Audet, M.
09/937484


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FILE 'REGISTRY' ENTERED AT 12:47:40 ON 02 JUN 2006
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STRUCTURE FILE UPDATES:    1 JUN 2006  HIGHEST RN 886490-27-3
DICTIONARY FILE UPDATES:   1 JUN 2006  HIGHEST RN 886490-27-3

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*                                                                    *
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on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html                    Search I
                                                              Erythrina
E1            1     ERYTHRINA CHYMOTRYPSIN INHIBITOR/CN
E2            1     ERYTHRINA CRISTA-GALLI, EXT./CN
E3            0 --> ERYTHRINA LECTIN/CN
E4            1     ERYTHRINADIENONE/CN
E5            1     ERYTHRINAN/CN

=> s e2
L1            1 "ERYTHRINA CRISTA-GALLI, EXT."/CN

FILE 'HCAPLUS' ENTERED AT 12:47:52 ON 02 JUN 2006
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FILE COVERS 1907 - 2 Jun 2006 VOL 144 ISS 24
FILE LAST UPDATED: 1 Jun 2006 (20060601/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON "ERYTHRINA CRISTA-GALLI, EXT."/CN
L2 298 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 OR ERYTHRINA(S)(LECTIN OR CRISTAGALLI OR CRISTA GALLI) OR ECL(S)ERYTHRINA
L3 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L2 AND (C OR NERVE)(3A)(FIBER OR FIBRE)

L3 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 06 Oct 2000
ACCESSION NUMBER: 2000:706999 HCAPLUS
DOCUMENT NUMBER: 133:261538
TITLE: Use of a lectin or lectin conjugate for modulation of **C-fiber** activity, and therapeutic use thereof
INVENTOR(S): Foster, Keith Alan; Chaddock, John Andrew; Quinn, Conrad Padraig
PATENT ASSIGNEE(S): Microbiological Research Authority, UK
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000057897	A1	20001005	WO 2000-GB1247	20000331
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2368641	AA	20001005	CA 2000-2368641	20000331
EP 1165114	A1	20020102	EP 2000-914295	20000331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 776281	B2	20040902	AU 2000-35690	20000331
PRIORITY APPLN. INFO.:			GB 1999-7429 A	19990331
			WO 2000-GB1247 W	20000331

AB The invention relates to the treatment of pain and to compds. that modulate **C-fiber** activity. In particular, the invention relates to the use of a lectin in the manufacture of a medicament for modulation of **C-fiber** neuron activity, and to lectin conjugates. The lectin conjugates comprise a lectin coupled to

a peptide or protein, wherein the peptide or protein is substantially free of Clostridial neurotoxin enzyme activity. The invention also concerns methods for manufacturing the conjugates. The compds. and compns. described have particular application in the treatment of diseases of which **C-fiber** activity is a component. Such diseases include pain, inflammation, psoriasis and other **C-fiber** related conditions.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 16 Dec 2001
ACCESSION NUMBER: 1940:36580 HCAPLUS
DOCUMENT NUMBER: 34:36580
ORIGINAL REFERENCE NO.: 34:5534c-d
TITLE: Action of so-called curarizing substances on the motor end plates
AUTHOR(S): Rojas, P.; Szepsenwol, J.; Resta, L. S.
SOURCE: Comptes Rendus des Seances de la Societe de Biologie et de Ses Filiales (1940), 133, 332-3
CODEN: CRSBAW; ISSN: 0037-9026
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C. A. 33, 6955.7. In the lizard, Teius teius, injection of cobra venom produced a slight enlargement of the motor nerve plates of the muscle cells but no retraction of the connecting **nerve fiber** endings. Extract of **Erythrina crista galli** did not affect the size of the plates but caused a slight retraction of the connecting **nerve fibers.** Veratrine caused a marked retraction and swelling of the **nerve fibers.**

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L4 4 S L3
L5 4 DUP REM L4 (0 DUPLICATES REMOVED)

L5 ANSWER 1 OF 4 MEDLINE on STN

ACCESSION NUMBER: 2004134201 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15027053
TITLE: Retargeted clostridial endopeptidases: inhibition of nociceptive neurotransmitter release in vitro, and antinociceptive activity in in vivo models of pain.
AUTHOR: Chaddock John A; Purkiss John R; Alexander Frances C G; Doward Sarah; Fooks Sarah J; Friis Lorna M; Hall Yper H J; Kirby Elizabeth R; Leeds Nicola; Moulsdale Hilary J; Dickenson Anthony; Green G Mark; Rahman Wahida; Suzuki Rie; Duggan Michael J; Quinn Conrad P; Shone Clifford C; Foster Keith A
CORPORATE SOURCE: Health Protection Agency, Porton Down, Salisbury, Wiltshire, United Kingdom.. john.chaddock@hpa.org.uk
SOURCE: Movement disorders : official journal of the Movement Disorder Society, (2004 Mar) Vol. 19 Suppl 8, pp. S42-7.
Journal code: 8610688. ISSN: 0885-3185.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 18 Mar 2004
Last Updated on STN: 16 Jun 2004
Entered Medline: 15 Jun 2004

AB Clostridial neurotoxins potently and specifically inhibit neurotransmitter release in defined cell types. Previously reported data have demonstrated that the catalytically active LH(N) endopeptidase fragment of botulinum neurotoxin type A (termed LH(N)/A) can be retargeted to a range of cell types in vitro to lead to inhibition of secretion of a range of transmitters. Here, we report the synthesis of endopeptidase conjugates with in vitro selectivity for nociceptive afferents compared to spinal neurons. Chemical conjugates prepared between **Erythrina cristagalli lectin** and LH(N)/A are assessed in vitro and in in vivo models of pain. Chemical conjugates prepared between E. cristagalli lectin and either natively sourced LH(N)/A, or recombinant LH(N)/A purified from Escherichia coli are assessed, and equivalence of the recombinant material is demonstrated. The duration of action of inhibition of neurotransmitter release by the conjugate in vitro is also assessed and is comparable to that observed with Clostridium botulinum neurotoxin. Selectivity of targeting and therapeutic potential have been confirmed by in vivo electrophysiology studies. Furthermore, the analgesic properties of the conjugate have been assessed in in vivo models of pain and extended duration effects observed. These data provide proof of principle for the concept of retargeted clostridial endopeptidases as novel analgesics.

L5 ANSWER 2 OF 4 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-611684 [58] WPIDS
DOC. NO. CPI: C2000-183090
TITLE: Manufacturing a medicament for modulating **C -fiber** neurone activity and treating e.g. pain, psoriasis, inflammation or mucus hypersecretion, comprises using a lectin or a nucleic acid encoding a lectin.
DERWENT CLASS: B04 D16
INVENTOR(S): CHADDOCK, J A; FOSTER, K A; QUINN, C P
PATENT ASSIGNEE(S): (MICR-N) MICROBIOLOGICAL RES AUTHORITY; (HEAL-N)

HEALTH PROTECTION AGENCY
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000057897	A1	20001005	(200058)*	EN	62
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000035690	A	20001016	(200106)		
EP 1165114	A1	20020102	(200209)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2002540162	W	20021126	(200307)		55
AU 776281	B2	20040902	(200477)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000057897	A1	WO 2000-GB1247	20000331
AU 2000035690	A	AU 2000-35690	20000331
EP 1165114	A1	EP 2000-914295	20000331
		WO 2000-GB1247	20000331
JP 2002540162	W	JP 2000-607647	20000331
		WO 2000-GB1247	20000331
AU 776281	B2	AU 2000-35690	20000331

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000035690	A	Based on	WO 2000057897
EP 1165114	A1	Based on	WO 2000057897
JP 2002540162	W	Based on	WO 2000057897
AU 776281	B2	Previous Publ.	AU 2000035690
		Based on	WO 2000057897

PRIORITY APPLN. INFO: GB 1999-7429 19990331
AN 2000-611684 [58] WPIDS
AB WO 200057897 A UPAB: 20001114
NOVELTY - Manufacturing (M1) a medicament for modulation of **C-fiber** neurone activity using a lectin.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) manufacturing (M2) a medicament for modulation of **C-fiber** neurone activity using a nucleic acid that encodes a lectin;

(2) a pharmaceutical composition comprising a lectin, where the composition is free of Clostridial neurotoxin enzyme activity;

(3) a composition comprising one or more nucleic acid sequences encoding lectins;

(4) a conjugate comprising a lectin coupled to a peptide or protein that is free of Clostridial neurotoxin enzyme activity and optionally has a **C-fiber** modulation activity;

(5) a nucleic acid encoding (4);

(6) manufacturing (M3) a medicament for modulation of **C -fiber** activity, using (2), (3), (4), or (5);

(7) treating pain, psoriasis, inflammation or mucus hypersecretion using a medicament manufactured with a lectin or a nucleic acid encoding a lectin;

(8) inhibiting **C-fiber** activity using a composition of (M1), (M2), or (M3);

(9) stimulating **C-fiber** activity using a composition of (M1), (M2), or (M3);

(10) modulating **C-fiber** activity comprising administering a lectin, (2), (3), (4) or (5) to a patient;

(11) preparing (4) comprising coupling together, optionally via a linker, a lectin and a peptide or protein; and

(12) preparing (4) comprising expressing (5) in a hart, optionally including a linker nucleic acid sequence located within (5) to provide a linker molecule between the lectin and the peptide or protein of the conjugate.

ACTIVITY - Analgesic; antipsoriatic; antiinflammatory; mucolytic; antiasthmatic; antiulcer; antiarthritic; antiallergic; antimigraine. The analgesic effects of a galactosyl-reactive lectin IB4 from Bandeiraea simplicifolia were studied in vivo, in adult outbred mice (MF1) of either sex,with a weight range of 10 - 30 g. The mice were anaesthetized and a 5 mm incision was made in the skin above the spinal column. Lectin IB4 was injected in a single dose into an intrathecal space. The incision was closed using a single wound clip and the mice became fully mobile within two minutes. The effect over a 10 hour period was monitored. A significant increase in withdrawal latency was observed at 1 hour post application with an apparent maximal activity at 4 hours (15.0 and 17.6 seconds, respectively, compared to 11.6 and 12.4 seconds for a control group injected with phosphate buffered saline (PBS)). Analgesia was still clearly discernable over control-group animals at 10 hours post application (15.7 seconds for IB4 injected animals and 12.7 seconds for PBS-injected animals).

MECHANISM OF ACTION - Substance P release modulator; **C-fiber** activity modulator. Embryonic dorsal rot ganglia (eDRG) were prepared from rats. An **Erythrina cristagalli lectin**-protein conjugate was applied to the eDRG and the substance P released was assayed. The percent inhibition of release was about 5 % at a concentration of 0.1 micro g/ml and was -45 % at 10 micro g/ml of the conjugate, demonstrating that the conjugate modulated release of substance P from an in vitro model of **C -fibers.**

USE - The new method is used for manufacturing a medicament for modulating **C-fiber** neurone activity, using a lectin or nucleic acid encoding a lectin (claimed). The medicament can be used to treat pain, psoriasis, inflammation or mucus hypersecretion (claimed). It can also be used to treat asthma, ulcer formation, headache, migraine, arthritis, and irritable bowel syndrome.

Dwg.0/14

L5 ANSWER 3 OF 4 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1998:704685 SCISEARCH
THE GENUINE ARTICLE: 119WD
TITLE: Lectin binding patterns in the vomeronasal organ and accessory olfactory bulb of the rat
AUTHOR: Salazar I (Reprint); Quinteiro P S
CORPORATE SOURCE: Univ Santiago de Compostela, Fac Vet, Dept Anat &

Embriol, E-27002 Lugo, Spain (Reprint)
COUNTRY OF AUTHOR: Spain
SOURCE: ANATOMY AND EMBRYOLOGY, (OCT 1998) Vol. 198, No. 4, pp. 331-339.
ISSN: 0340-2061.
PUBLISHER: SPRINGER-VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010 USA

DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 54
ENTRY DATE: Entered STN: 1998
Last Updated on STN: 1998
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A number of previous studies have indicated that lectin histochemistry is an obvious choice for characterizing the vomeronasal system. However, apparently inconsistent results have been obtained: notably, the affinity with which Various lectins bind to the accessory olfactory bulb varies among taxa, even considering closely related species. In the present study, the binding patterns of seven lectins in the rat accessory olfactory bulb, vomeronasal nerves and vomeronasal duct were investigated. The Bandeiraea simplicifolia lectin bound exclusively to the vomeronasal nerve and glomerular layers of the accessory olfactory bulb, while the Ulex europeus and Lycopersicon esculentum lectins bound to these regions and additionally to the nerve and glomerular layers of the main olfactory bulb. Soybean agglutinin showed a similar pattern to that obtained with the Ulex europeus and Lycopersicon esculentum lectins, though it also faintly labelled other parts of the structures examined. The Vicia villosa and **Erythrina cristagalli lectins** were not specific for the vomeronasal system, since they labelled grey and white matters in structures including the lateral olfactory tract and the anterior olfactory nuclei. The Dolichos biflorus lectin did not bind to vomeronasal tissues. The observed patterns of binding in the accessory olfactory bulb were consistent with those observed in the vomeronasal nerves, but unlike those observed in the epithelium of the vomeronasal duct. This latter result probably reflects binding of lectins to sugar residues contained in secreted mucus rather than those in epithelial nerve endings.

L5 ANSWER 4 OF 4 EMBASE
ACCESSION NUMBER: 92081343 EMBASE
DOCUMENT NUMBER: 1992081343
TITLE: Bandeiraea simplicifolia lectin I and Vicia villosa agglutinin bind specifically to the vomeronasal axons in the accessory olfactory bulb of the rat.
AUTHOR: Ichikawa M.; Osada T.; Ikai A.
CORPORATE SOURCE: Department of Anatomy and Embryology, Tokyo Metropolitan Institute for Neuroscience, 2-6 Musashidai, Fuchu, Tokyo 183, Japan
SOURCE: Neuroscience Research, (1992) Vol. 13, No. 1, pp. 73-79. .
ISSN: 0168-0102 CODEN: NERADN
COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 001 Anatomy, Anthropology, Embryology and Histology
008 Neurology and Neurosurgery
011 Otorhinolaryngology
LANGUAGE: English

SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 17 Apr 1992
Last Updated on STN: 17 Apr 1992

AB The binding of 21 lectins to the accessory olfactory bulb (AOB) of the rat was examined by histochemistry. Two lectins [Bandeiraea simplicifolia lectins I (BSL-I and Vicia villosa agglutinin (VVA)] bound specifically to the vomeronasal (VN) axons in the AOB. Seven **lectins** (Datura stramonium **lectin**, **Erythrina cristagalli lectin**, Lycoperisicon esculentum **lectin**, Ricinus communis agglutinin I, soybean agglutinin, Solanum tuberosum **lectin**, and Ulex europaeus agglutinin) bound to both VN axons in AOB and olfactory axons in the main olfactory bulb. BSL-I and VVA are useful as the marker of VN axons. This selective binding of lectins indicates the presence of specific glycoconjugates on the surface of VN axons

FILE 'HCAPLUS' ENTERED AT 12:50:38 ON 02 JUN 2006
L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON "ERYTHRINA CRISTA-GALLI, EXT."/CN
L2 298 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 OR ERYTHRINA(S)(LECTIN OR CRISTAGALLI OR CRISTA GALLI) OR ECL(S)ERYTHRINA
L6 11 SEA FILE=HCAPLUS ABB=ON PLU=ON L2 AND (PAIN OR ACHE OR INFLAMMAT? OR PSORIASIS OR ASTHMA OR ULCER OR HEADACHE OR MUCUS(3A)(HYPERSECRET? OR HYPER SECRET?) OR PUSTUL? OR HEMICRANIA## OR HEMI CRANIA## OR CEPHALGIA)
L7 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L6 AND (TREAT? OR THERAP? OR PREVENT?)

L8 5 L7 NOT L3

L8 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 23 Sep 2005
ACCESSION NUMBER: 2005:1027067 HCAPLUS
DOCUMENT NUMBER: 143:321814
TITLE: High throughput glycan microarrays for diagnosis and compositions of glycans for immunization and **therapy**
INVENTOR(S): Blixt, Ola; Head, Steve
PATENT ASSIGNEE(S): The Scripps Research Institute, USA
SOURCE: PCT Int. Appl., 228 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005088310	A2	20050922	WO 2005-US7370	20050307
WO 2005088310	A3	20051124		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,

DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-550667P P 20040305

US 2004-558598P P 20040331

US 2004-629833P P 20041119

AB The invention provides arrays of glycans for detecting entities that bind to glycans. In some embodiments, the arrays can be used to detect disease, blood types, antibodies, bacterial or viral infection, cancer, and the like. The invention also provides methods and kits for such detection. In another embodiment, the invention provides methods of **preventing** or **treating** disease in a mammal by administering to the mammal a composition that includes at least glycan.

L8 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 18 Aug 2005
ACCESSION NUMBER: 2005:813134 HCAPLUS
DOCUMENT NUMBER: 144:146169
TITLE: Metabolites from endophytes of the medicinal plant **Erythrina crista-galli**
AUTHOR(S): Weber, Daniela; Gorzalczany, Susana; Martino, Virginia; Acevedo, Cristina; Sterner, Olov; Anke, Timm
CORPORATE SOURCE: Institut fuer Biotechnologie und Wirkstoff-Forschung IBWF, Kaiserslautern, D-67663, Germany
SOURCE: Zeitschrift fuer Naturforschung, C: Journal of Biosciences (2005), 60(5/6), 467-477
CODEN: ZNCBDA; ISSN: 0939-5075
PUBLISHER: Verlag der Zeitschrift fuer Naturforschung
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Erythrina crista-galli** (Fabaceae) is used in Argentinean ethnopharmacol. as anti-**inflammatory** medication, narcotic, desinfectant, and for the **treatment** of wounds. The common name of the tree is "ceibo" or coral tree. The dominating endophytes in E. crista-galli all belong to the genus Phomopsis as identified by microscopic features and the anal. of their ITS sequences. To investigate a possible contribution of Phomopsis spp. to the metabolites found in the plant, twelve different isolates were cultivated in different media. Besides several new metabolites a number of known compds. were detected: mellein, nectriapyrone, 4-hydroxymellein, scytalone, tyrosol, clavatol, mevinic acid, and mevalonolactone.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 24 Sep 2002
ACCESSION NUMBER: 2002:721252 HCAPLUS
DOCUMENT NUMBER: 138:1236
TITLE: Inhibition of Release of Neurotransmitters from Rat Dorsal Root Ganglia by a Novel Conjugate of a Clostridium botulinum Toxin A Endopeptidase Fragment and **Erythrina**

cristagalli Lectin

AUTHOR(S): Duggan, Michael J.; Quinn, Conrad P.; Chaddock, John A.; Purkiss, John R.; Alexander, Frances C. G.; Doward, Sarah; Fooks, Sarah J.; Friis, Lorna M.; Hall, Yper H. J.; Kirby, Elizabeth R.; Leeds, Nicola; Moulsdale, Hilary J.; Dickenson, Anthony; Green, G. Mark; Rahman, Wahida; Suzuki, Rie; Shone, Clifford C.; Foster, Keith A.

CORPORATE SOURCE: Centre for Applied Microbiology and Research, Porton Down, Salisbury, Wiltshire, SPR 0JG, UK

SOURCE: Journal of Biological Chemistry (2002), 277(38), 34846-34852
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Clostridial neurotoxins potently and specifically inhibit neurotransmitter release in defined cell types. Here we report that a catalytically active derivative (termed LHN/A) of the type A neurotoxin from Clostridium botulinum has been coupled to a **lectin** obtained from **Erythrina cristagalli** to form a novel conjugate. This conjugate exhibits an in vitro selectivity for nociceptive afferents compared with the anatomically adjacent spinal neurons, as assessed using in vitro primary neuronal culture systems to measure inhibition of release of neurotransmitters. Chemical conjugates prepared between E. cristagalli lectin and either natively sourced LHN/A or recombinant LHN/A purified from Escherichia coli are assessed, and equivalence of the recombinant material are demonstrated. Furthermore, the dependence of inhibition of neurotransmitter release on the cleavage of SNAP-25 is demonstrated through the use of an endopeptidase-deficient LHN/A conjugate variant. The duration of action of inhibition of neurotransmitter released by the conjugate in vitro is assessed and is comparable with that observed with Clostridium botulinum neurotoxin. Finally, in vivo electrophysiol. shows that these in vitro actions have biol. relevance in that sensory transmission from nociceptive afferents through the spinal cord is significantly attenuated. These data demonstrate that the potent endopeptidase activity of clostridial neurotoxins can be selectively retargeted to cells of interest and that inhibition of release of neurotransmitters from a neuronal population of **therapeutic** relevance to the **treatment** of **pain** can be achieved.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 23 Apr 1999

ACCESSION NUMBER: 1999:249106 HCAPLUS

DOCUMENT NUMBER: 130:276767

TITLE: Conjugates of galactose-binding lectins and clostridial neurotoxins as analgesics

INVENTOR(S): Duggan, Michael John; Chaddock, John Andrew

PATENT ASSIGNEE(S): The Speywood Laboratory Limited, UK; Microbiological Research Authority

SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9917806	A1	19990415	WO 1998-GB3001	19981007
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2306350	AA	19990415	CA 1998-2306350	19981007
AU 9893574	A1	19990427	AU 1998-93574	19981007
AU 741456	B2	20011129		
ZA 9809138	A	19990527	ZA 1998-9138	19981007
EP 996468	A1	20000503	EP 1998-946571	19981007
EP 996468	B1	20030521		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001518522	T2	20011016	JP 2000-514674	19981007
AT 240747	E	20030615	AT 1998-946571	19981007
PT 996468	T	20030930	PT 1998-946571	19981007
ES 2198750	T3	20040201	ES 1998-946571	19981007
US 7052702	B1	20060530	US 2000-529130	20000622
PRIORITY APPLN. INFO.:			GB 1997-21189 A	19971008
			WO 1998-GB3001 W	19981007

AB A class of novel agents that are able to modify nociceptive afferent function is provided. The agents may inhibit the release of neurotransmitters from discrete populations of neurons and thereby reduce or preferably **prevent** the transmission of afferent **pain** signals from peripheral to central **pain** fibers. They comprise a galactose-binding lectin linked to a derivative of a clostridial neurotoxin. The derivative of the clostridial neurotoxin comprises the L-chain, or a fragment thereof, which includes the active proteolytic enzyme domain of the light (L) chain, linked to a mol. or domain with membrane-translocating activity. The agents may be used in or as pharmaceuticals for the **treatment** of **pain**, particularly chronic **pain**.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 28 Nov 1996
ACCESSION NUMBER: 1996:705679 HCAPLUS
DOCUMENT NUMBER: 125:339039
TITLE: Microcapsules of pre-determined peptide(s) specificity(ies), their preparation and uses
INVENTOR(S): Speaker, Tully J.; Sultzbaugh, Kenneth J.
PATENT ASSIGNEE(S): Temple University, USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9629059	A1	19960926	WO 1996-US3666	19960318
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5686113	A	19971111	US 1995-408052	19950321
CA 2212744	AA	19960926	CA 1996-2212744	19960318
AU 9653148	A1	19961008	AU 1996-53148	19960318
EP 817617	A1	19980114	EP 1996-909753	19960318
EP 817617	B1	20030514		
R: DE, FR, GB, IT				
JP 11502817	T2	19990309	JP 1996-528543	19960318
PRIORITY APPLN. INFO.:			US 1995-408052 A	19950321
			WO 1996-US3666 W	19960318

AB An aqueous core microcapsule has a capsular wall provided with a peptide(s) of pre-determined binding specificity(ies) appended to the surface, the wall being the reaction product of an anionic polymer or salt thereof and a polyamine, salt thereof, mixts. thereof, or mixts. thereof with monoamines. The aqueous core may contain an active ingredient(s), and be targeted for delivery to specific cell tissues. The microcapsules are provided as a composition and in a kit with instructions for use in imaging, diagnosis, **therapy**, vaccination, and other applications. Spermine/alginate microcapsules were prepared by addition of nominally 8 + 10-7 μL droplets of a 0.05% (weight/volume) aqueous Na alginate solution to a 0.05% (weight/volume) aqueous spermine-HCl solution at room temperature The resulting suspension of microcapsules was stirred to allow equilibration and then allowed to settle, the supernatant was removed, and microcapsules washed and stored at refrigerator temperature

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 12:51:57 ON 02 JUN 2006)

L9 15 S L7
L10 13 S L9 NOT L4
L11 8 DUP REM L10 (5 DUPLICATES REMOVED)

L11 ANSWER 1 OF 8 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:323483 SCISEARCH
THE GENUINE ARTICLE: 024NW
TITLE: Clostridial neurotoxins: structure-function led design of new **therapeutics**
AUTHOR: Chaddock J A (Reprint); Marks P M H
CORPORATE SOURCE: Hlth Protect Agcy, Ctr Emergency Preparedness & Response, Salisbury SP4 0JG, Wilts, England (Reprint) john.chaddock@hpa.org.uk
COUNTRY OF AUTHOR: England
SOURCE: CELLULAR AND MOLECULAR LIFE SCIENCES, (MAR 2006) Vol. 63, No. 5, pp. 540-551.
ISSN: 1420-682X.
PUBLISHER: BIRKHAUSER VERLAG AG, VIADUKSTRASSE 40-44, PO BOX 133,

CH-4010 BASEL, SWITZERLAND.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 99
ENTRY DATE: Entered STN: 7 Apr 2006
Last Updated on STN: 7 Apr 2006
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The neurotoxins produced by various species of Clostridia are the causative agents of botulism and tetanus. The ability of the toxins, specifically those of the botulinum neurotoxin family, to disrupt neurotransmission has been exploited for use in several medical indications and now represents the **therapeutic** option of choice in a number of cases. Clostridial neurotoxins have been discovered to have a multi-domain structure that is shared between the various proteins of the family, and it has also been determined that each domain contributes a specific role to the holotoxin. The extensive use of recombinant expression approaches, along with solution of multiple crystallographic structures of individual domains, has enabled researchers to explore structurefunction relationships of the toxin domains more closely. These advances have facilitated a greater understanding of the potential use of individual domains for a wide variety of purposes, including the development of new **therapeutics.**

L11 ANSWER 2 OF 8 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2005384469 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16042349
TITLE: Metabolites from endophytes of the medicinal plant **Erythrina crista-galli.**
AUTHOR: Weber Daniela; Gorzalczany Susana; Martino Virginia; Acevedo Cristina; Sterner Olov; Anke Timm
CORPORATE SOURCE: Institut fur Biotechnologie und Wirkstoff-Forschung, Kaiserslautern, Germany.
SOURCE: Zeitschrift fur Naturforschung. C, Journal of biosciences, (2005 May-Jun) Vol. 60, No. 5-6, pp. 467-77.
Journal code: 8912155. ISSN: 0341-0382.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200510
ENTRY DATE: Entered STN: 27 Jul 2005
Last Updated on STN: 19 Oct 2005
Entered Medline: 18 Oct 2005

AB **Erythrina crista-galli** (Fabaceae) is used in Argentinean ethnopharmacology as anti-**inflammatory** medication, narcotic, desinfectant, and for the **treatment** of wounds. The common name of the tree is "ceibo" or coral tree. The dominating endophytes in E. crista-galli all belong to the genus Phomopsis as identified by microscopic features and the analysis of their ITS sequences. To investigate a possible contribution of Phomopsis spp. to the metabolites found in the plant, twelve different isolates were cultivated in different media. Besides several new metabolites a number of known compounds were detected: mellein, nectriapyrone, 4-hydroxymellein, scytalone, tyrosol, clavatol, mevinic acid, and mevalonolactone.

L11 ANSWER 3 OF 8 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:1020901 SCISEARCH
THE GENUINE ARTICLE: 870LQ
TITLE: The analgesic potential of clostridial neurotoxin derivatives
AUTHOR: Foster K A (Reprint)
CORPORATE SOURCE: HPA Porton Down, Salisbury SP4 0JG, Wilts, England (Reprint)
keith.foster@hpa.org.uk
COUNTRY OF AUTHOR: England
SOURCE: EXPERT OPINION ON INVESTIGATIONAL DRUGS, (NOV 2004) Vol. 13, No. 11, pp. 1437-1443.
ISSN: 1354-3784.
PUBLISHER: ASHLEY PUBLICATIONS LTD, UNITEC HOUSE, 3RD FL, 2 ALBERT PLACE, FINCHLEY CENTRAL, LONDON N3 1QB, ENGLAND
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 45
ENTRY DATE: Entered STN: 16 Dec 2004
Last Updated on STN: 16 Dec 2004
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Botulinum neurotoxins are the most potent acute lethal toxins known, and yet for the last two decades they, and in particular serotype A, have found increasing use in the clinical **treatment** of diseases or conditions involving neuromuscular or autonomic neuronal transmission. The neurotoxins work by inhibiting the release of acetylcholine from peripheral cholinergic nerve terminals. More recently, the effects on non-cholinergic pathways have been identified, and this has led to an increase in the diseases and syndromes for which botulinum neurotoxins have been found to have clinical utility. In particular, botulinum neurotoxins have been demonstrated to potentially benefit a range of chronic **pain** syndromes. With the description in the last decade of the biochemical basis of neurotoxin action and the tertiary structure of the toxin molecule, the possibility of designing novel agents utilising selected aspects of toxin function has arisen. This possibility has been pursued in the context of **pain** relief with the description of a novel hybrid protein derived from botulinum neurotoxin type A, LHN/A-ECL, able to selectively target nociceptive afferent neurons and inhibit the release of neurotransmitters involved in **pain** transmission. This novel derivative of botulinum neurotoxin type A demonstrates prolonged analgesic activity in vivo. This review will consider the evidence for the analgesic properties of the botulinum neurotoxins and their suitability as the basis for novel **therapeutic** proteins. The general concept of deriving novel **therapeutic** molecules from the neurotoxins will also be considered.

L11 ANSWER 4 OF 8 MEDLINE on STN
ACCESSION NUMBER: 2004607395 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15580955
TITLE: Phomol, a new antiinflammatory metabolite from an endophyte of the medicinal plant **Erythrina crista-galli.**
AUTHOR: Weber Daniela; Sterner Olov; Anke Timm; Gorzalczancy Susanna; Martino Virginia; Acevedo Christina
CORPORATE SOURCE: Institute of Biotechnology and Drug Research, Erwin-Schrodinger-Str. 56, D-67663 Kaiserslautern, Germany.
SOURCE: The Journal of antibiotics, (2004 Sep) Vol. 57, No. 9,

pp. 559-63.
Journal code: 0151115. ISSN: 0021-8820.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 8 Dec 2004
Last Updated on STN: 4 Jan 2005
Entered Medline: 3 Jan 2005

AB Phomol (1), a novel antibiotic, was isolated from fermentations of a Phomopsis species in the course of a screening of endophytic fungi from the medicinal plant **Erythrina crista-galli.** For this Argentinean leguminosa antiinflammatory and neuroleptic activities have been described. The compound exhibits antifungal, antibacterial and weak cytotoxic acticity. The antiinflammatory activity was tested in different reporter gene assays (TNF-alpha, STAT1/STAT2 and NF-kappaB) and in an ear edema model in mice. In the reporter gene assays 1 exhibited no activity, whereas 1 showed interesting antiinflammatory activity in the mouse ear assay. The compound is a polyketide lactone and its structure was elucidated by spectroscopic methods.

L11 ANSWER 5 OF 8 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:284444 SCISEARCH
THE GENUINE ARTICLE: 803KX
TITLE: Retargeted clostridial endopeptidases: Inhibition of nociceptive neurotransmitter release in vitro, and antinociceptive activity in in vivo models of **pain**
AUTHOR: Chaddock J A (Reprint); Purkiss J R; Alexander F C G; Doward S; Fooks S J; Friis L M; Hall Y H J; Kirby E R; Leeds N; Moulsdale H J; Dickenson A; Green G M; Rahman W; Suzuki R; Duggan M J; Quinn C P; Shone C C; Foster K A
CORPORATE SOURCE: Hlth Protect Agcy, Porton Down, Salisbury SP4 0JG, Wilts, England (Reprint); Hlth Protect Agcy, Salisbury SP4 0JG, Wilts, England; Univ Coll London, London, England
COUNTRY OF AUTHOR: England
SOURCE: MOVEMENT DISORDERS, (MAR 2004) Vol. 19, Supp. [8], pp. S42-S47.
ISSN: 0885-3185.
PUBLISHER: WILEY-LISS, DIV JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 22
ENTRY DATE: Entered STN: 2 Apr 2004
Last Updated on STN: 2 Apr 2004
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Clostridial neurotoxins potently and specifically inhibit neurotransmitter release in defined cell types. Previously reported data have demonstrated that the catalytically active LHN endopeptidase fragment of botulinum neurotoxin type A (termed LHN/A) can be retargeted to a range of cell types in vitro to lead to inhibition of secretion of a range of transmitters. Here, we report the synthesis of endopeptidase conjugates with in vitro selectivity for nociceptive afferents compared to spinal neurons. Chemical conjugates prepared

between **Erythrina cristagalli lectin** and LHN/A are assessed in vitro and in in vivo models of **pain.** Chemical conjugates prepared between E. cristagalli lectin and either natively sourced LHN/A, or recombinant LHN/A purified from Escherichia coli are assessed, and equivalence of the recombinant material is demonstrated. The duration of action of inhibition of neurotransmitter release by the conjugate in vitro is also assessed and is comparable to that observed with Clostridium botulinum neurotoxin. Selectivity of targeting and **therapeutic** potential have been confirmed by in vivo electrophysiology studies. Furthermore, the analgesic properties of the conjugate have been assessed in in vivo models of **pain** and extended duration effects observed. These data provide proof of principle for the concept of retargeted clostridial endopeptidases as novel analgesics. (C) 2004 Movement Disorder Society.

L11 ANSWER 6 OF 8 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004316705 EMBASE

TITLE: Retargeted clostridial endopeptidases: Inhibition of nociceptive neurotransmitter release in vitro, and antinociceptive activity in vivo models of **pain** .

AUTHOR: Chaddock J.A.; Purkiss J.R.; Alexander F.C.G.; Doward S.; Fooks S.J.; Friis L.M.; Hall Y.H.J.; Kirby E.R.; Leeds N.; Moulsdale H.J.; Dickenson A.; Green G.M.; Rahman W.; Suzuki R.; Duggan M.J.; Quinn C.P.; Shone C.C.; Foster K.A.

CORPORATE SOURCE: Dr. J.A. Chaddock, Health Protection Agency, Porton Down, Salisbury, Wiltshire SP4 0JG, United Kingdom. john.chaddock@hpa.org.uk

SOURCE: Movement Disorders, (2004) Vol. 19, No. SUPPL. 8, pp. S42-S47. .
Refs: 22
ISSN: 0885-3185 CODEN: MOVDEA

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology
008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 12 Aug 2004
Last Updated on STN: 12 Aug 2004

AB Clostridial neurotoxins potently and specifically inhibit neurotransmitter release in defined cell types. Previously reported data have demonstrated that the catalytically active LH(N) endopeptidase fragment of botulinum. neurotoxin type A (termed LH(N)/A) can be retargeted to a range of cell types in vitro to lead to inhibition of secretion of a range of transmitters. Here, we report the synthesis of endopeptidase conjugates with in vitro selectivity for nociceptive afferents compared to spinal neurons. Chemical conjugates prepared between **Erythrina cristagalli lectin** and LH(N)/A are assessed in vitro and in in vivo models of **pain.** Chemical conjugates prepared between E. cristagalli lectin and either natively sourced LH(N)/A, or recombinant LH(N)/A purified from Escherichia coli are assessed, and equivalence of the recombinant material is demonstrated. The duration of action of inhibition of neurotransmitter release by the conjugate

in vitro is also assessed and is comparable to that observed with Clostridium botulinum neurotoxin. Selectivity of targeting and **therapeutic** potential have been confirmed by in vivo electrophysiology studies. Furthermore, the analgesic properties of the conjugate have been assessed in in vivo models of **pain** and extended duration effects observed. These data provide proof of principle for the concept of retargeted clostridial endopeptidases as novel analgesics. .COPYRGT. 2004 Movement Disorder Society.

L11 ANSWER 7 OF 8 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2002470902 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12105193
TITLE: Inhibition of release of neurotransmitters from rat dorsal root ganglia by a novel conjugate of a Clostridium botulinum toxin A endopeptidase fragment and **Erythrina cristagalli lectin.**
AUTHOR: Duggan Michael J; Quinn Conrad P; Chaddock John A; Purkiss John R; Alexander Frances C G; Doward Sarah; Fooks Sarah J; Friis Lorna M; Hall Yper H J; Kirby Elizabeth R; Leeds Nicola; Moulsdale Hilary J; Dickenson Anthony; Green G Mark; Rahman Wahida; Suzuki Rie; Shone Clifford C; Foster Keith A
CORPORATE SOURCE: Centre for Applied Microbiology and Research, Porton Down, Salisbury, Wiltshire SP4 0JG, United Kingdom.
SOURCE: The Journal of biological chemistry, (2002 Sep 20) Vol. 277, No. 38, pp. 34846-52. Electronic Publication: 2002-07-08.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 17 Sep 2002
Last Updated on STN: 5 Jan 2003
Entered Medline: 24 Oct 2002

AB Clostridial neurotoxins potently and specifically inhibit neurotransmitter release in defined cell types. Here we report that a catalytically active derivative (termed LH(N)/A) of the type A neurotoxin from Clostridium botulinum has been coupled to a **lectin** obtained from **Erythrina cristagalli** to form a novel conjugate. This conjugate exhibits an in vitro selectivity for nociceptive afferents compared with the anatomically adjacent spinal neurons, as assessed using in vitro primary neuronal culture systems to measure inhibition of release of neurotransmitters. Chemical conjugates prepared between E. cristagalli lectin and either natively sourced LH(N)/A or recombinant LH(N)/A purified from Escherichia coli are assessed, and equivalence of the recombinant material are demonstrated. Furthermore, the dependence of inhibition of neurotransmitter release on the cleavage of SNAP-25 is demonstrated through the use of an endopeptidase-deficient LH(N)/A conjugate variant. The duration of action of inhibition of neurotransmitter released by the conjugate in vitro is assessed and is comparable with that observed with Clostridium botulinum neurotoxin. Finally, in vivo electrophysiology shows that these in vitro actions have biological relevance in that sensory transmission from nociceptive afferents through the spinal cord is significantly attenuated. These data demonstrate that the potent endopeptidase activity of clostridial neurotoxins can be selectively retargeted to cells of interest and

that inhibition of release of neurotransmitters from a neuronal population of **therapeutic** relevance to the **treatment** of **pain** can be achieved.

L11 ANSWER 8 OF 8 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 1999-263908 [22] WPIDS
DOC. NO. CPI: C1999-077843
TITLE: Conjugate of lectin and clostridial neurotoxin fragment.
DERWENT CLASS: B04 D16
INVENTOR(S): CHADDOCK, J A; DUGGAN, M J
PATENT ASSIGNEE(S): (MICR-N) MICROBIOLOGICAL RES AUTHORITY; (SPEY-N) SPEYWOOD LAB LTD
COUNTRY COUNT: 85
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9917806	A1	19990415	(199922)*	EN	49
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
ZA 9809138	A	19990728	(199935)		48
AU 9893574	A	19990427	(199936)		
EP 996468	A1	20000503	(200026)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
JP 2001518522	W	20011016	(200176)		52
AU 741456	B	20011129	(200206)		
EP 996468	B1	20030521	(200341)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
DE 69814858	E	20030626	(200350)		
ES 2198750	T3	20040201	(200414)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9917806	A1	WO 1998-GB3001	19981007
ZA 9809138	A	ZA 1998-9138	19981007
AU 9893574	A	AU 1998-93574	19981007
EP 996468	A1	EP 1998-946571	19981007
		WO 1998-GB3001	19981007
JP 2001518522	W	WO 1998-GB3001	19981007
		JP 2000-514674	19981007
AU 741456	B	AU 1998-93574	19981007
EP 996468	B1	EP 1998-946571	19981007
		WO 1998-GB3001	19981007
DE 69814858	E	DE 1998-614858	19981007
		EP 1998-946571	19981007
		WO 1998-GB3001	19981007
ES 2198750	T3	EP 1998-946571	19981007

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9893574	A	Based on	WO 9917806

EP 996468	A1	Based on	WO 9917806
JP 2001518522	W	Based on	WO 9917806
AU 741456	B	Previous Publ.	AU 9893574
		Based on	WO 9917806
EP 996468	B1	Based on	WO 9917806
DE 69814858	E	Based on	EP 996468
		Based on	WO 9917806
ES 2198750	T3	Based on	EP 996468

PRIORITY APPLN. INFO: GB 1997-21189 19971008
AN 1999-263908 [22] WPIDS
AB WO 9917806 A UPAB: 19990609
NOVELTY - Agent (A) for **treating pain** comprises a galactose-binding lectin (I) linked to a derivative (II) of a clostridial neurotoxin (CN), i.e. the light (L) chain, or its fragment that retains the active proteolytic enzyme domain, linked to a molecule or domain (IIa) with membrane translocating activity.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method for obtaining (A), and

(2) the use of (A) for **treating pain.**

ACTIVITY - Analgesic.

MECHANISM OF ACTION - (A) **prevent**, or control, release (exocytosis) of neurotransmitters and neuromodulators from primary sensory or nociceptive afferents, so control transmission of **pain** from the periphery to the central nervous system. Primary cultures of rat dorsal root ganglia were incubated with a conjugate of the lectin from Erythria cristagalli with a fragment of botulinum toxin type A containing the L chain and the N-terminal part of the heavy chain. The concentration of conjugate required for 50% inhibition of release of the neurotransmitters glutamate and substance P was 3.66 mu g/ml.

USE - (A) are used to alleviate or **prevent pain** , especially severe chronic **pain**, e.g. where associated with malignancies.

ADVANTAGE - (A) can be targeted to particular populations of afferent neurons, depending on the nature of (I).

Dwg.0/10

Search II
Lectin

FILE 'REGISTRY' ENTERED AT 12:54:07 ON 02 JUN 2006
E LECTIN/CN 5
E LECTINS/CN 5
L12 664 S (LECTINS OR LECTIN ?)/CN

FILE 'HCAPLUS' ENTERED AT 12:54:34 ON 02 JUN 200
L12 664 SEA FILE=REGISTRY ABB=ON PLU=ON (LECTINS OR LECTIN ?)/CN

L13 40420 SEA FILE=HCAPLUS ABB=ON PLU=ON L12 OR LECTIN OR ISOLECTIN

L14 90 SEA FILE=HCAPLUS ABB=ON PLU=ON L13 AND (C OR NERVE)(3A)(F IBER OR FIBRE)

L15 34 SEA FILE=HCAPLUS ABB=ON PLU=ON L14 AND (PAIN OR ACHE OR INFLAMMAT? OR PSORIASIS OR ASTHMA OR ULCER OR HEADACHE OR MUCUS(3A)(HYPERSECRET? OR HYPER SECRET?) OR PUSTUL? OR HEMICRANIA## OR HEMI CRANIA## OR CEPHALGIA)

L16 14 SEA FILE=HCAPLUS ABB=ON PLU=ON L15 AND (TREAT? OR THERAP? OR MODULAT? OR PREVENT? OR INHIBIT?)

L17 13 L16 NOT (L3 OR L7)

L17 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 14 Mar 2006
ACCESSION NUMBER: 2006:227171 HCAPLUS
DOCUMENT NUMBER: 144:344025
TITLE: Spinal nerve ligation does not alter the expression or function of GABAB receptors in spinal cord and dorsal root ganglia of the rat
AUTHOR(S): Engle, M. P.; Gassman, M.; Sykes, K. T.; Bettler, B.; Hammond, D. L.
CORPORATE SOURCE: Department of Anesthesia, The University of Iowa, Iowa City, IA, 52242, USA
SOURCE: Neuroscience (San Diego, CA, United States) (2006), 138(4), 1277-1287
CODEN: NRSCDN; ISSN: 0306-4522
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Loss of GABA-mediated **inhibition** in the spinal cord is thought to mediate allodynia and spontaneous **pain** after nerve injury. Despite extensive investigation of GABA itself, relatively little is known about how nerve injury alters the receptors at which GABA acts. This study examined levels of GABAB receptor protein in the spinal cord dorsal horn, and in the L4 and L5 (lumbar designations) dorsal root ganglia one to 18 wk after L5 spinal nerve ligation. Mech. allodynia was maximal by 1 wk and persisted at blunted levels for at least 18 wk after injury. Spontaneous **pain** behaviors were evident for 6 wk. Western blotting of dorsal horn detected two isoforms of the GABAB(1) subunit and a single GABAB(2) subunit. High levels of GABAB(1a) and low levels of GABAB(1b) protein were present in the dorsal root ganglia. However, GABAB(2) protein was not detected in the dorsal root ganglia, consistent with the proposed existence of an atypical receptor composed of GABAB(1) homodimers. The levels of GABAB(1a), GABAB(1b), and GABAB(2) protein in the ipsilateral dorsal horn were unchanged at any time after injury. Immunohistochem. staining also did not detect a change in GABAB(1) or GABAB(2) subunits in dorsal horn segments having a robust loss of **isolectin** B4 staining. The levels of GABAB(1a) protein were also unchanged in the L4 or L5 dorsal root ganglia at any time after spinal nerve ligation. Levels of GABAB(2) remained undetectable. Finally, baclofen-stimulated binding of guanosine-5'-(γ-O-thio)triphosphate in dorsal horn did not differ between sham and ligated rats. Collectively, these results argue that a loss of GABAB receptor-mediated **inhibition**, particularly of central terminals of primary afferents, is unlikely to mediate the development or maintenance of allodynia or spontaneous **pain** behaviors after spinal nerve injury.
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 10 Oct 2005
ACCESSION NUMBER: 2005:1080085 HCAPLUS
DOCUMENT NUMBER: 144:105869
TITLE: A fluorescent double labeled observation of NMDAR1 and BSI-B4 in the spinal dorsal horn of the **inflammation**-induced rat and its electroacupuncture **modulation**
AUTHOR(S): Zhang, Yuwen; Wang, Lina; Li, Man; Zhang, Jing;

Li, Lingli; Guan, Xinmin
CORPORATE SOURCE: Tongji Medical College, Huazhong University of Science and Technology, Wuhan, 430030, Peop. Rep. China
SOURCE: Jiepou Xuebao (2005), 36(1), 32-36
CODEN: CPHPA5; ISSN: 0529-1356
PUBLISHER: Jiepou Xuebao Bianji Weiyuanhui
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The change of N-methyl-D-aspartate (NMDA) receptor NR1 to primary afferent **C fiber** in the spinal dorsal horn of the rat following **inflammatory pain** was studied. The Sprague-Dawley rats were divided into control group (n=12), **inflammation** group (n=12) and electroacupuncture (EA) **treatment** group (n=12). EA was done in acupoints "Huan Tiao" (GB30) and "Yang Lin Quan" (GB34) (stimulation indexes: 0.5-1.5V, 4-16 Hz, 30 min) following injection of Complete Freund's adjuvant (CFA). Using immunoflourescence histochem. double-staining technique, the distributions and relationships between Banderaea Simplicifolia **Isolectin** B4 (BSI-B4) labeled primary afferent **C fibers** and terminals and NR1 in the dorsal root ganglion (DRG) and superficial laminae of the spinal dorsal horn following CFA-induced **inflammation** and EA **treatment** were analyzed. NR1 was located in primary afferent **C fibers** and terminals of both DRG and superficial laminae of the spinal dorsal horn. In addition, in the DRG, at 3rd d and 7th d following injection of CFA, the percentages of the number of double-labeled cells to the total number of the BSI-B4 labeled cells and NR1 immunoreactive cells, resp., all showed that: **inflammation** group>EA **treatment** group>control group ($P<0.01$), and 3rd group>7th group ($P<0.05$). The results suggested that NR1 was located in primary afferent **C fibers** and terminals, and the up-regulation and activation of this presynaptic NR1 may contribute significantly to the hyperalgesia that accompanies persistent **inflammation.** Moreover, EA **treatment** could down-regulate the NR1 expression following **inflammation** to analgesia consequently.

L17 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 24 May 2005
ACCESSION NUMBER: 2005:436726 HCAPLUS
DOCUMENT NUMBER: 143:260070
TITLE: Ablation of primary afferent terminals reduces nicotinic receptor expression and the nociceptive responses to nicotinic agonists in the spinal cord
AUTHOR(S): Khan, Imran M.; Wennerholm, Michelle; Singletary, Erin; Polston, Kimberley; Zhang, Limin; Deerinck, Tom; Yaksh, Tony L.; Taylor, Palmer
CORPORATE SOURCE: Department of Pharmacology, University of California, San Diego, CA, 92093-0636, USA
SOURCE: Journal of Neurocytology (2005), Volume Date 2004, 33(5), 543-556
CODEN: JNCYA2; ISSN: 0300-4864
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A variety of studies indicate that spinal nicotinic acetylcholine receptors **modulate** the behavioral and autonomic responses elicited by afferent stimuli. To examine the location of and role played by particular subtypes of nicotinic receptors in mediating

cardiovascular and nociceptive responses, we **treated** neonatal and adult rats with capsaicin to destroy **C-fibers** in primary afferent terminals. Reduction of **C-fiber** terminals was ascertained by the loss of **isolectin** B4, CGRP and vanilloid receptors as monitored by immunofluorescence. Receptor autoradiog. shows a reduction in number of epibatidine binding sites following capsaicin **treatment.** The reduction is particularly marked in the dorsal horn and primarily affects the class of high affinity epibatidine binding sites thought to **modulate** nociceptive responses. Accompanying the loss of terminals and nicotinic binding sites were significant redns. in the expression of α3, α4, α5, β2 and β4 nicotinic receptor subunits in the superficial layers of the spinal cord as determined by antibody staining and confocal microscopy. The loss of nicotinic receptors that follows capsaicin **treatment** results in attenuation of the nociceptive responses to both spinal cytisine and epibatidine. Capsaicin **treatment** also diminishes the capacity of cytisine to desensitize nicotinic receptors mediating nociception, but it shows little effect on intrathecal nicotinic agonist elicited pressor and heart rate responses. Hence, our data suggest that α3, α4, α5, β2 and β4 subunits of nicotinic receptors are localized in the spinal cord on primary afferent terminals that mediate nociceptive input. A variety of convergent data based on functional studies and subunit expression suggest that α3 and α4, in combination with β2 and α5 subunits, form the majority of functional nicotinic receptors on **C-fiber** primary afferent terminals. Conversely, spinal nicotinic receptors not located on **C-fibers** play a primary role in the spinal pathways evoking spinally coordinated autonomic cardiovascular responses.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 16 Apr 2004
ACCESSION NUMBER: 2004:312287 HCAPLUS
DOCUMENT NUMBER: 140:315072
TITLE: Methods and compounds for the **treatment** of **mucus hypersecretion** by **inhibiting mucus** secretion using compounds having targeting and translocating modified light chain of clostridial neurotoxin
INVENTOR(S): Quinn, Conrad Padraig; Foster, Keith Alan; Chaddock, John
PATENT ASSIGNEE(S): Health Protection Agency, USA
SOURCE: U.S. Pat. Appl. Publ., 19 pp., Cont.-in-part of U.S. 6,632,440.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004071736	A1	20040415	US 2003-633698	20030805
WO 2000010598	A2	20000302	WO 1999-GB2806	19990825
WO 2000010598	A3	20000615		
W: AU, CA, JP, US				

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

US 6632440	B1	20031014	US 2001-763669		20010529
PRIORITY APPLN. INFO.:			GB 1998-18548	A	19980825
			WO 1999-GB2806	W	19990825
			US 2001-763669	A2	20010529

AB A method of **treating mucus hypersecretion**, the causative factor in chronic obstructive pulmonary disease (COPD), **asthma** and other clin. conditions involving COPD, comprises administering a compound that **inhibits** exocytosis in mucus secreting cells or neurons that control or direct mucus secretion. Also described is a compound, for use in the **treatment** of **hypersecretion** of **mucus**, which **inhibits** mucus secretion by **inhibiting** mucus secretion by mucus secreting cells, and/or **inhibiting** neurotransmitter release from neuronal cells controlling or directing mucus secretion. The compound comprises: (a) a light chain (L-chain) or L-chain fragment of a clostridial neurotoxin, which L-chain or L-chain fragment includes the active proteolytic enzyme domain of the L-chain; (b) a targeting domain that binds to a target cell selected from the group consisting of (i) a mucus secreting cell, and (ii) a neuronal cell controlling or directing mucus secretion; and (c) a translocating domain that translocates the L-chain or L-chain fragment into the target cell; with the proviso that the compound is not a botulinum toxin. Substance P, as the targeting domain, was conjugated to clostridial neurotoxin fragment LHN/A.

L17 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 21 Dec 2003
ACCESSION NUMBER: 2003:991382 HCAPLUS
DOCUMENT NUMBER: 140:31455
TITLE: **Therapeutic** conjugate consisting of a MEK **inhibitor** and a targeting agent
INVENTOR(S): Lee, Kevin; Ho, Michael Ting Bong
PATENT ASSIGNEE(S): Cambridge Biotechnology Ltd., UK
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003103717	A1	20031218	WO 2003-GB2501	20030611
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003240080	A1	20031222	AU 2003-240080	20030611

PRIORITY APPLN. INFO.: GB 2002-13383 A 20020611

WO 2003-GB2501 W 20030611

AB Conjugates for use in the **treatment** of **pain**, particularly chronic **pain** are described. The conjugates comprise a MEK **inhibitor** and a targeting agent. The targeting agent targets the MEK **inhibitor** to sensory neurons, thereby reducing the dosage of MEK **inhibitor** required to **treat** chronic **pain**. Methods of **treating** chronic **pain** using the conjugates are also described.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 22 Oct 2003
ACCESSION NUMBER: 2003:828902 HCAPLUS
DOCUMENT NUMBER: 140:87993
TITLE: Distribution of antinociceptive adenosine A1 receptors in the spinal cord dorsal horn, and relationship to primary afferents and neuronal subpopulations
AUTHOR(S): Schulte, G.; Robertson, B.; Fredholm, B. B.; DeLander, G. E.; Shortland, P.; Molander, C.
CORPORATE SOURCE: Department of Neuroscience, Karolinska Institutet, Stockholm, SE-171 77, Swed.
SOURCE: Neuroscience (Oxford, United Kingdom) (2003), 121(4), 907-916
CODEN: NRSCDN; ISSN: 0306-4522
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Adenosine can reduce **pain** and allodynia in animals and man, probably via spinal adenosine A1 receptors. In the present study, the authors investigate the distribution of the adenosine A1 receptor in the rat spinal cord dorsal horn using immunohistochem., in situ hybridization, radioligand binding, and confocal microscopy. In the lumbar cord dorsal horn, dense immunoreactivity was seen in the inner part of lamina II. This was unaltered by dorsal root section or thoracic cord hemisection. Confocal microscopy of the dorsal horn revealed close anatomical relationships but no or only minor overlap between A1 receptors and immunoreactivity for markers associated with primary afferent central endings: calcitonin gene-related peptide, or **isolectin** B4, or with neuronal subpopulations: μ-opioid receptor, neuronal nitric oxide synthase, met-enkephalin, parvalbumin, or protein kinase Cγ, or with glial cells: glial fibrillary acidic protein. A few adenosine A1 receptor pos. structures were double-labeled with α-amino-3-hydroxy-5-methyl-4-isoaxolepropionic acid glutamate receptor subunits 1 and 2/3. The results indicate that most of the adenosine A1 receptors in the dorsal horn are located in inner lamina II postsynaptic neuronal cell bodies and processes whose functional and neurochem. identity is so far unknown. Many adenosine A1 receptor pos. structures are in close contact with **isolectin** B4 pos. **C-fiber** primary afferents and/or postsynaptic structures containing components of importance for the **modulation** of nociceptive information.

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L17 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 24 Apr 2003
ACCESSION NUMBER: 2003:314474 HCAPLUS
DOCUMENT NUMBER: 139:147130
TITLE: Resiniferatoxin induces paradoxical changes in thermal and mechanical sensitivities in rats: Mechanism of action
AUTHOR(S): Pan, Hui-Lin; Khan, Ghous M.; Alloway, Kevin D.; Chen, Shao-Rui
CORPORATE SOURCE: Department of Anesthesiology, The Milton S. Hershey Medical Center, The Pennsylvania State University College of Medicine, Hershey, PA, 17033-0850, USA
SOURCE: Journal of Neuroscience (2003), 23(7), 2911-2919
CODEN: JNRSDS; ISSN: 0270-6474
PUBLISHER: Society for Neuroscience
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Resiniferatoxin (RTX), an ultrapotent analog of capsaicin, has been used as a tool to study the role of capsaicin-sensitive **C fibers** in **pain.** Recently, we found that RTX diminished the thermal sensitivity but unexpectedly increased the sensitivity to tactile stimulation in adult rats. In this study, we explored the potential mechanisms involved in RTX-induced changes in somatosensory function. An i.p. injection of 200 μg/kg RTX, but not its vehicle, rapidly produced an increase in the paw withdrawal latency to a heat stimulus. Also, profound tactile allodynia developed in all the RTX-**treated** rats in 3 wk. This paradoxical change in thermal and mech. sensitivities lasted for at least 6 wk. Electron microscopic examination of the sciatic nerve revealed a loss of unmyelinated fibers and extensive ultrastructural damage of myelinated fibers in RTX-**treated** rats. Immunofluorescence labeling showed a diminished vanilloid receptor 1 immunoreactivity in dorsal root ganglia neurons and the spinal dorsal horn of RTX-**treated** rats. Furthermore, two transganglionic tracers, horseradish peroxidase conjugates of cholera toxin B subunit (CTB) and **isolectin**-B4 of Bandeiraea simplicifolia (IB4), were injected into the opposite sides of the sciatic nerve to trace myelinated and unmyelinated afferent terminations, resp., in the spinal dorsal horn. In RTX-**treated** rats, IB4-labeled terminals in the dorsal horn were significantly reduced, and CTB-labeled terminals appeared to sprout into lamina II of the spinal dorsal horn. Thus, this study demonstrates that systemic RTX diminishes the thermal **pain** sensitivity by depletion of unmyelinated afferent neurons. The delayed tactile allodynia induced by RTX is likely attributable to damage to myelinated afferent fibers and their abnormal sprouting in lamina II of the spinal dorsal horn. These data provide new insights into the potential mechanisms of postherpetic neuralgia.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 27 Nov 2001
ACCESSION NUMBER: 2001:856429 HCAPLUS
DOCUMENT NUMBER: 136:194605
TITLE: The expression of bradykinin B1 receptors on primary sensory neurones that give rise to small

caliber sciatic **nerve fibres** in rats

AUTHOR(S): Ma, Q.-P.

CORPORATE SOURCE: Department of Pharmacology, Merck Sharp & Dohme Research Laboratories, Neuroscience Research Centre, Harlow, CM20 2QR, UK

SOURCE: Neuroscience (Oxford, United Kingdom) (2001), 107(4), 665-673
CODEN: NRSCDN; ISSN: 0306-4522

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The bradykinin B1 receptor has been considered as an important mediator for **inflammatory pain.** In the present study, the authors have investigated the **fiber** types of sciatic **nerve** primary sensory neurons that express B1 receptors by retrograde tracing in combination with immunohistochem. staining, or double-immunohistochem. staining. Approx. 12% of the A-fiber dorsal root ganglion neurons, retrogradely labeled from an intra-sciatic nerve injection of fluorescein isothiocyanate-conjugated cholera toxin B subunit, were B1 receptor-immunoreactive. Over 70% of the small diameter dorsal root ganglion neurons, retrogradely labeled from an intra-sciatic nerve injection of tetramethylrhodamine isothiocyanate-conjugated wheat germ agglutinin, were B1 receptor-immunoreactive. Over 50% of the (predominantly non-peptidergic) **C-fiber** dorsal root ganglion neurons, retrogradely labeled from an intra-sciatic nerve injection of fluorescein isothiocyanate-conjugated Bandeiraea simplicifolia **isolectin** B4, were B1 receptor-immunoreactive. When calcitonin gene-related peptide, which is contained mainly in small caliber **C**- and Aδ- **fiber** primary afferents, and B1 receptors were stained with a double-immunofluorescent method, over 80% of the calcitonin gene-related peptide-pos. dorsal root ganglion neurons were B1 receptor-immunoreactive. From these results the authors suggest that B1 receptors are predominantly expressed by small diameter primary afferent neurons that give rise to sciatic **nerve fibers**, which include both peptidergic and non-peptidergic **C-fibers** and Aδ-fibers. Since peripheral nociceptive information is primarily transmitted by **C**- and Aδ- **fibers**, B1 receptors may be involved in the **modulation** of nociceptive transduction or transmission.

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 24 May 2001

ACCESSION NUMBER: 2001:373190 HCAPLUS

DOCUMENT NUMBER: 135:221614

TITLE: ATP affects both axons and Schwann cells of unmyelinated **C fibres**

AUTHOR(S): Irnich, D.; Burgstahler, R.; Bostock, H.; Grafe, P.

CORPORATE SOURCE: Department of Anesthesiology, University of Munich, Munich, D-81377, Germany

SOURCE: Pain (2001), 92(3), 343-350
CODEN: PAINDB; ISSN: 0304-3959

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Recent studies indicate that effects of ATP on unmyelinated afferent **nerve fibers** contribute to the transduction of nociceptive and non-nociceptive stimuli. In the present study, effects of ATP were studied on axons and Schwann cells of **C fibers** in isolated rat vagus nerves. A combination of a computerized threshold tracking technique with photometric and confocal measurements of the free intracellular Ca2+ concentration revealed differences in the effect of ATP and related compds. Pyridoxal-phosphate-6-azophenyl-2',5'-disulfonic acid (iso-PPADS, an antagonist of ionotropic P2X receptors) completely blocked the excitatory effect of α,β-meATP on unmyelinated axons, whereas the effects of ATP and 2-Cl-ATP were only slightly changed. Moreover, the threshold lowering effects of ATP and 2-Cl-ATP, but not of α,β-meATP, were accompanied by intracellular Ca2+ transients. In confocal imaging expts., the **lectin** IB4 was used to identify unmyelinated **nerve fibers** and their ensheathing Schwann cells. The Schwann cells were identified as the cellular elements underlying ATP-induced Ca2+ transients. In addition, an increase in axonal excitability of **C fibers** was seen during a rise in [Ca2+]i induced by **inhibition** of the endoplasmic Ca2+ ATPase with cyclopiazonic acid. These data show that an increase of the extracellular ATP concentration in an intact peripheral nerve trunk activates both axons and Schwann cells. It appears that P2 nucleotide receptors on Schwann cells may contribute to the excitatory effect of ATP observed on unmyelinated, including nociceptive, axons.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 06 Dec 2000

ACCESSION NUMBER: 2000:853555 HCAPLUS

DOCUMENT NUMBER: 134:66519

TITLE: Localization of N-methyl-D-aspartate NR2B subunits on primary sensory neurons that give rise to small-caliber sciatic **nerve fibers** in rats

AUTHOR(S): Ma, Q.-P.; Hargreaves, R. J.

CORPORATE SOURCE: Department of Pharmacology, Merck Sharp & Dohme Research Laboratories, Neuroscience Research Centre, Terlings Park, Harlow, CM20 2QR, UK

SOURCE: Neuroscience (Oxford) (2000), 101(3), 699-707
CODEN: NRSCDN; ISSN: 0306-4522

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In the present study the authors have used immunohistochem. staining and retrograde tracing techniques to investigate the relationship between the N-methyl-D-aspartate receptor NR2B subunits and small-diameter primary afferent dorsal root ganglion neurons that give rise to the sciatic **nerve fibers.** Three days after an intra-sciatic nerve injection of tetra-Me rhodamine isothiocyanate-conjugated wheat germ agglutinin which labels small-diameter primary afferents, many NR2B and wheat germ agglutinin-double-labeled cells (.apprx.70% of wheat germ agglutinin-labeled neurons) were observed in the L5 dorsal root ganglia. Three days after an intra-sciatic nerve injection of fluorescein isothiocyanate-conjugated Bandeiraea simplicifolia agglutinin

isolectin B4 which labels predominantly non-peptidergic **C-fiber** primary afferents, NR2B and Bandeiraea simplicifolia agglutinin **isolectin** B4 double-labeled neurons (.apprx.90% of Bandeiraea simplicifolia agglutinin **isolectin** B4-labeled neurons) were also observed in the L5 dorsal root ganglion. Three days after an intra-sciatic nerve injection of fluorescein isothiocyanate-conjugated cholera toxin B subunit, only .apprx.40% of cholera toxin B subunit-labeled neurons were NR2B pos. and those labeled neurons tended to be small-sized. When calcitonin gene-related peptide and NR2B were labeled by a double immunofluorescent staining technique, the authors found that the majority of calcitonin gene-related peptide-pos. neurons was NR2B immunoreactive (>90% of calcitonin gene-related peptide-pos. neurons, and .apprx.60% of NR2B-pos. neurons) as well. Size frequency anal. also demonstrated that NR2B subunits were predominantly localized on the small and medium-sized neurons. These results suggest that NR2B subunits are predominantly expressed on small diameter primary afferents, and these NR2B containing N-methyl-D-aspartate receptors may play a role in the **modulation** of neurotransmitter release from primary afferent terminals.

REFERENCE COUNT: 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 31 Oct 2000
ACCESSION NUMBER: 2000:760879 HCAPLUS
DOCUMENT NUMBER: 134:37278
TITLE: Morphological evidences for presynaptic **inhibitory** effect of neurotensin on primary afferent **C fiber** in the spinal dorsal horn of the rat
AUTHOR(S): Li, He; Zhang, Yinon; Zhang, Minhai; Yang, Shiming; Li, Honglian
CORPORATE SOURCE: Department of Histology and Embryology, Tongji Medical University, Wuhan, 430030, Peop. Rep. China
SOURCE: Zhongguo Zuzhi Huaxue Yu Xibao Huaxue Zazhi (2000), 9(2), 229-235, plate P-8
CODEN: ZZXZFZ; ISSN: 1004-1850
PUBLISHER: Zhongguo Zuzhi Huaxue Yu Xibao Huaxue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of the present study is to reveal whether neurotensin (NT) in the spinal dorsal horn of the rat might presynaptically **modulate** the primary afferent **C fibers.** With fluorescence microscope, it was observed that, in the laminae I-III of the spinal cord, the distribution of neurotensin-like immunoreactivity (NTLI) was partially overlapped with that of the binding of **isolectin** I-B4 from Griffonia simplicifolia (I-B4). The further observation with confocal laser scanning microscope showed that a few of NTLI-pos. terminals contacted with some I-B4-labeled terminals. It was found electron microscopically in the superficial layers of the spinal cord of the rat **treated** with subarachnoid injection of capsaicin that NTLI-containing terminals contacted with degenerated terminals with and/or without synaptic specializations. These results indicate that NT may presynaptically **inhibit** the transmission of primary afferent **C fibers** via axoaxonic synapses and/or nonsynaptic contacts.

Addnl., axodendritic synapses between degenerated terminals and NTLI-containing dendrites also exist in the spinal dorsal horn.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 08 May 1998
ACCESSION NUMBER: 1998:263079 HCAPLUS
DOCUMENT NUMBER: 129:1013
TITLE: A distinct subgroup of small DRG cells express GDNF receptor components and GDNF is protective for these neurons after nerve injury
AUTHOR(S): Bennett, David L. H.; Michael, Gregory J.; Ramachandran, Navin; Munson, John B.; Averill, Sharon; Yan, Qiao; McMahon, Stephen B.; Priestley, John V.
CORPORATE SOURCE: Department of Physiology, United Medical and Dental Schools, London, SE1 7EH, UK
SOURCE: Journal of Neuroscience (1998), 18(8), 3059-3072
CODEN: JNRSDS; ISSN: 0270-6474
PUBLISHER: Society for Neuroscience
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several lines of evidence suggest that neurotrophin administration may be of some **therapeutic** benefit in the **treatment** of peripheral neuropathy. However, a third of sensory neurons do not express receptors for the neurotrophins. These neurons are of small diameter and can be identified by the binding of the **lectin** IB4 and the expression of the enzyme thiamin monophosphatase (TMP). These neurons express the receptor components for glial-derived neurotrophic factor (GDNF) signaling (RET, GFRα-1, and GFRα-2). In lumbar dorsal root ganglia, virtually all IB4-labeled cells express RET mRNA, and the majority of these cells (79%) also express GFRα-1, GFRα-2, or GFRα-1 plus GFRα-2. GDNF, but not nerve growth factor (NGF), can **prevent** several axotomy-induced changes in these neurons, including the downregulation of IB4 binding, TMP activity, and somatostatin expression. GDNF also **prevents** the slowing of conduction velocity that normally occurs after axotomy in a population of small diameter DRG cells and the A-fiber sprouting into lamina II of the dorsal horn. GDNF therefore may be useful in the **treatment** of peripheral neuropathies and may protect peripheral neurons that are refractory to neurotrophin **treatment.**
REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 02 Jan 1996
ACCESSION NUMBER: 1996:2866 HCAPLUS
DOCUMENT NUMBER: 124:83862
TITLE: Changes in neuronal markers in a mononeuropathic rat model: Relationship between neuropeptide Y, pre-emptive drug **treatment** and long-term mechanical hyperalgesia
AUTHOR(S): Munglani, R.; Bond, A.; Smith, G. D.; Harrison, S. M.; Elliot, P. J.; Birch, P. J.; Hunt, S. P.
CORPORATE SOURCE: Clinical School, University Cambridge, Cambridge, CB2 2QQ, UK

SOURCE: Pain (1995), 63(1), 21-31
CODEN: PAINDB; ISSN: 0304-3959
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Using the chronic constriction model (CCI) of Bennett and Xie (1988), changes in the lumbar spinal cord in neuropeptides and **lectin** IB4 were examined at 28 days post-nerve constriction and were compared with the degree of mech. hyperalgesia. Animals following nerve ligation were significantly more hyperalgesic than sham-operated animals. **Lectin** IB4, a marker of primary afferent **C fibers**, showed a qual. decrease in staining intensity in laminae 1-2 with ligation compared with both the unoperated contralateral side and with sham animals. Using fluorescent immunohistochem. to quantify changes in neuropeptides in the dorsal horn the authors found that substance P showed significant decreases with ligation compared to sham operation. CGRP and galanin showed no significant changes in laminae 1-2 compared to sham-operated animals. Neuropeptide Y (NPY) showed no significant changes in intensity in laminae 1-2; however, in laminae 3-4 there was a significant increase with nerve ligation compared to sham. The authors examined how pre-emptive drug **treatment** affected these neuronal markers at 28 days. The authors used (1) clonidine, an α2-adrenoreceptor agonist (1 mg/kg, i.p.), (2) morphine, a μ-opioid agonist (5 mg/kg, i.p.) or (3) MK-801, an N-methyl-D-aspartate (NMDA) receptor antagonist (0.3 mg/kg, s.c.) administered 30 min prior and 6 h following nerve ligation or sham-operation. Hyperalgesia in the ligated group at 28 days was suppressed by **treatment** with pre-emptive clonidine or MK-801 but not morphine. With the exception of NPY there was no effect of pre-emptive drug **treatment** on any neuronal marker examined Pre-emptive MK-801 reduced the magnitude of the increase in NPY in laminae 3-4 in the ligated group and clonidine showed a similar trend but this did not reach significance. Morphine had no effect on NPY staining. There was a significant correlation between the increase in NPY staining in laminae 3-4 and the degree of hyperalgesia (r = 0.6). These results suggest that the increased NPY expression in laminae 3-4 of the spinal cord (the territory of the myelinated sensory input) may be crucial to the development of hyperalgesia in this model.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 13:03:45 ON 02 JUN 2006)

L18 54 S L16
L19 52 S L18 NOT (L4 OR L9)
L20 32 DUP REM L19 (20 DUPLICATES REMOVED)

L20 ANSWER 1 OF 32 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:217243 SCISEARCH
THE GENUINE ARTICLE: 896RM
TITLE: alpha 2-adrenoceptors **inhibit** the intracellular Ca2+ response to electrical stimulation in normal and injured sensory neurons, with increased **inhibition** of calcitonin gene-related peptide expressing neurons after injury
AUTHOR: Eisenach J C (Reprint); Zhang Y; Duflo F
CORPORATE SOURCE: Wake Forest Univ, Sch Med, Dept Anesthesiol, Ctr Study Pharmacol Plastic Presence Pain, Med Ctr Blvd, Winston Salem, NC 27157 USA (Reprint); Wake Forest Univ, Sch Med, Dept Anesthesiol, Ctr Study Pharmacol Plastic

Presence Pain, Winston Salem, NC 27157 USA
eisenach@wfubmc.edu
COUNTRY OF AUTHOR: USA
SOURCE: NEUROSCIENCE, (2005) Vol. 131, No. 1, pp. 189-197.
ISSN: 0306-4522.
PUBLISHER: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 52
ENTRY DATE: Entered STN: 3 Mar 2005
Last Updated on STN: 3 Mar 2005
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Nerve injury resulting in chronic **pain** is associated with novel excitatory effects of norepinephrine on injured peripheral nerve terminals and their cell bodies, due to actions on alpha2-adrenoceptors. Paradoxically, alpha2-adrenoceptor agonists administered near peripheral terminals or their cell bodies results in analgesia, not **pain.** This study tested, using intracellular Ca2+ response to stimulation, the effects of alpha2-adrenoceptor agonists on injured sensory neurons and classified their neuronal phenotype.

Dorsal root ganglion cells from normal and spinal nerveligated rats were dissociated and activated twice with electrical field stimulation, while measuring Fura-2 fluorescence. Cells were perfused between stimulations with vehicle or alpha2-adrenoceptor agonists alone or with antagonists. Cells were considered **inhibited** if the ratio of their peak Ca2+ response to the second stimulus divided by the first was less than the 2.5th percentile for vehicle controls.

alpha2-, But not alpha1-adrenoceptor agonists **inhibited** the Ca2+ response in a concentration related fashion, and this **inhibition** was blocked by alpha2-adrenoceptor antagonists. Clonidine **inhibited** a similar percentage of cells in the normal and spinal nerveligated group. In both groups, the large majority of clonidine-**inhibited** cells stained for **isolectin** B4. Spinal nerve ligation resulted in a 4-10-fold increase in the percentage of clondine **inhibited** cells which immunostained for calcitonin gene-related peptide.

These data are consistent with the known **inhibition** of Ca2+ currents by alpha2-adrenoceptors and suggest that, at the level of intracellular Ca2+, the key determinant of neurotransmitter release, alpha2-adrenoceptors are **inhibitory** after nerve injury, not excitatory. There is a shift in phenotype of sensory neurons which are **inhibited** by clonidine after nerve injury, which may explain clonidine's increased potency in the **treatment** of neuropathic compared with acute **pain.**

L20 ANSWER 2 OF 32 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2005158041 EMBASE
TITLE: **Inflammation**-induced hyperexcitability of nociceptive gastrointestinal DRG neurones: The role of voltage-gated ion channels.
AUTHOR: Beyak M.J.; Vanner S.
CORPORATE SOURCE: Dr. S. Vanner, Hotel Dieu Hospital, 166 Brock St., Kingston, Ont. K7L 5G2, Canada. vanners@hdh.kari.net
SOURCE: Neurogastroenterology and Motility, (2005) Vol. 17, No. 2, pp. 175-186. .

Refs: 96
ISSN: 1350-1925 CODEN: NMOTEK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 002 Physiology
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 5 May 2005
Last Updated on STN: 5 May 2005

AB Gastrointestinal (GI) **inflammation modulates** the intrinsic properties of nociceptive dorsal root ganglia neurones, which innervate the GI tract and these changes are important in the genesis of abdominal **pain** and visceral hyperalgesia. neurones exhibit hyperexcitability characterized by a decreased threshold for activation and increased firing rate, and changes in voltage-gated Na(+) and K(+) channels play a major role in this plasticity. This review highlights emerging evidence that specific subsets of channels and signalling pathways are involved and their potential to provide novel selective **therapeutic** targets for the **treatment** of abdominal **pain.** .COPYRGT. 2004 Blackwell Publishing Ltd.

L20 ANSWER 3 OF 32 MEDLINE on STN
ACCESSION NUMBER: 2005263503 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15906161
TITLE: Ablation of primary afferent terminals reduces nicotinic receptor expression and the nociceptive responses to nicotinic agonists in the spinal cord.
AUTHOR: Khan Imran M; Wennerholm Michelle; Singletary Erin; Polston Kimberley; Zhang Limin; Deerinck Tom; Yaksh Tony L; Taylor Palmer
CORPORATE SOURCE: Department of Pharmacology, University of California, San Diego, CA 92093-0636, USA.. ikhan@ucsd.edu
CONTRACT NUMBER: HL-35018 (NHLBI)
SOURCE: Journal of neurocytology, (2004 Sep) Vol. 33, No. 5, pp. 543-56.
Journal code: 0364620. ISSN: 0300-4864.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200508
ENTRY DATE: Entered STN: 21 May 2005
Last Updated on STN: 31 Aug 2005
Entered Medline: 30 Aug 2005

AB A variety of studies indicate that spinal nicotinic acetylcholine receptors **modulate** the behavioral and autonomic responses elicited by afferent stimuli. To examine the location of and role played by particular subtypes of nicotinic receptors in mediating cardiovascular and nociceptive responses, we **treated** neonatal and adult rats with capsaicin to destroy **C-fibers** in primary afferent terminals. Reduction of **C-fiber** terminals was ascertained by the loss of **isolectin** B4, CGRP and vanilloid receptors as monitored by immunofluorescence. Receptor autoradiography shows a reduction in number of epibatidine binding sites following capsaicin **treatment.** The reduction is particularly marked in the dorsal horn and primarily affects the class of high affinity epibatidine binding sites thought to **modulate** nociceptive responses.

Accompanying the loss of terminals and nicotinic binding sites were significant reductions in the expression of alpha 3, alpha 4, alpha 5, beta 2 and beta 4 nicotinic receptor subunits in the superficial layers of the spinal cord as determined by antibody staining and confocal microscopy. The loss of nicotinic receptors that follows capsaicin **treatment** results in attenuation of the nociceptive responses to both spinal cytisine and epibatidine. Capsaicin **treatment** also diminishes the capacity of cytisine to desensitize nicotinic receptors mediating nociception, but it shows little effect on intrathecal nicotinic agonist elicited pressor and heart rate responses. Hence, our data suggest that alpha 3, alpha 4, alpha 5, beta 2 and beta 4 subunits of nicotinic receptors are localized in the spinal cord on primary afferent terminals that mediate nociceptive input. A variety of convergent data based on functional studies and subunit expression suggest that alpha 3 and alpha 4, in combination with beta 2 and alpha 5 subunits, form the majority of functional nicotinic receptors on **C-fiber** primary afferent terminals. Conversely, spinal nicotinic receptors not located on **C-fibers** play a primary role in the spinal pathways evoking spinally coordinated autonomic cardiovascular responses.

L20 ANSWER 4 OF 32 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:676553 SCISEARCH
THE GENUINE ARTICLE: 839FZ
TITLE: Effects of **isolectin** B4-conjugated saporin, a targeting cytotoxin, on bladder overactivity induced by bladder irritation
AUTHOR: Nishiguchi J; Sasaki K; Seki S; Chancellor M B; Erickson K A; de Groat W C; Kumon H; Yoshimura N (Reprint)
CORPORATE SOURCE: Univ Pittsburgh, Sch Med, Dept Urol, Pittsburgh, PA 15213 USA (Reprint); Univ Pittsburgh, Sch Med, Dept Pharmacol, Pittsburgh, PA 15213 USA; Okayama Univ, Grad Sch Med & Dent, Dept Urol, Okayama 7008558, Japan nyos@pitt.edu
COUNTRY OF AUTHOR: USA; Japan
SOURCE: EUROPEAN JOURNAL OF NEUROSCIENCE, (JUL 2004) Vol. 20, No. 2, pp. 474-482.
ISSN: 0953-816X.
PUBLISHER: BLACKWELL PUBLISHING LTD, 9600 GARSINGTON RD, OXFORD OX4 2DG, OXON, ENGLAND.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 31
ENTRY DATE: Entered STN: 20 Aug 2004
Last Updated on STN: 20 Aug 2004
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In order to clarify the functional role of the **isolectin** B4 (IB4)-binding afferent pathway in the micturition reflex, we investigated the effects on bladder activity of intrathecal application of the IB4-saporin conjugate, a targeting cytotoxin that destroys neurons binding IB4. In rats, IB4-saporin (2.5 mum) or vehicle was administered through an intrathecal catheter implanted at the level of the L6-S1 spinal cord. Three weeks after IB4-saporin administration, cystometry in conscious animals revealed a reduction in bladder overactive responses induced by intravesical capsaicin or ATP infusion without affecting normal voiding function. In histochemical studies, double staining for IB4 and saporin was

detected in L6 dorsal root ganglia (DRG) neurons 2 days after the **treatment**. Three weeks after the **treatment**, the area in lamina II of the L6 spinal cord stained with IB4 was significantly reduced compared with the area stained in control rats. The staining in the L1 spinal cord was not affected. The percentage of neurons in the L6 DRG intensely labeled with IB4 was also reduced in IB4-saporin-**treated** rats. These results indicate that intrathecal **treatment** with the IB4-saporin conjugate at the level of L6-S1 spinal cord, which reduces IB4 afferent nerve terminal staining in lamina II of the L6 spinal cord as well as the number of IB4-binding neurons in L6 DRG, suppressed bladder overactivity induced by bladder irritation without affecting normal micturition. Thus targeting IB4-binding, non-peptidergic afferent pathways sensitive to capsaicin and adenosine 5'-triphosphate may be an effective **treatment** for overactivity and/or **pain** responses in the bladder.

L20 ANSWER 5 OF 32 MEDLINE on STN
ACCESSION NUMBER: 2004319747 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15219679
TITLE: Ultrastructural analysis of the central terminals of primary sensory neurones labelled by transganglionic transport of bandeiraea simplicifolia I-**isolectin** B4.
AUTHOR: Gerke M B; Plenderleith M B
CORPORATE SOURCE: Neuroscience Laboratory, School of Life Sciences, Queensland University of Technology, Brisbane, Queensland, 4001, Australia.. mbgerke@med.usyd.edu.au
SOURCE: Neuroscience, (2004) Vol. 127, No. 1, pp. 165-75. Journal code: 7605074. ISSN: 0306-4522.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200410
ENTRY DATE: Entered STN: 29 Jun 2004
Last Updated on STN: 15 Oct 2004
Entered Medline: 14 Oct 2004

AB In this study the ultrastructural appearance of primary sensory neurones labelled by the injection of the plant **lectin** Bandeiraea simplicifolia I-**isolectin** B(4) (BSI-B(4)) into a peripheral nerve has been examined in the rat. Electron microscopy of the somata of retrogradely labelled neurones showed the **lectin** to be associated with the inner surface of cytoplasmic vesicles, supporting the premise that the uptake of BSI-B(4) into sensory neurones is by the process of receptor-mediated endocytosis. Light and electron microscopic analysis of the spinal cord revealed transganglionically transported **lectin** in unmyelinated axons in the dorsolateral funiculus and axon terminals concentrated mainly within lamina II of the dorsal horn. Detailed analysis of 1377 of these axon terminals revealed that the majority were glomerular in shape and surrounded by up to 14 other unlabelled profiles. These findings suggest that primary sensory neurones which transganglionically transport BSI-B(4) have a synaptic ultrastructure similar to that which has been previously reported for unmyelinated primary sensory neurones. Moreover, it appears that the axon terminals of these neurones are subjected to extensive **modulation**. Examination of the vesicle content of **lectin** labelled axon terminals revealed that the majority contained small agranular vesicles while large granular vesicles were

observed only occasionally. These findings support the suggestion that the populations of neurones expressing binding sites for BSI-B(4) are fairly distinct from those containing neuroactive peptides. In conclusion, the results of the current study suggest that the **lectin** BSI-B(4) can be used as a histological marker for a subpopulation of small diameter primary sensory neurones and provide further evidence for the potential of this **lectin** as a useful tool in the study of **pain.**

L20 ANSWER 6 OF 32 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-062228 [06] WPIDS
DOC. NO. CPI: C2004-025532
TITLE: Conjugate useful for the **prevention**, **treatment** or amelioration of arthritis, cancer or **pain** comprises a mitogen activated protein kinases kinase **inhibitor** and a targeting agent.
DERWENT CLASS: B04 D16
INVENTOR(S): HO, M T B; LEE, K
PATENT ASSIGNEE(S): (CAMB-N) CAMBRIDGE BIOTECHNOLOGY LTD
COUNTRY COUNT: 102
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003103717	A1	20031218	(200406)*	EN	17

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

AU 2003240080	A1	20031222	(200445)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003103717	A1	WO 2003-GB2501	20030611
AU 2003240080	A1	AU 2003-240080	20030611

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003240080	A1 Based on	WO 2003103717

PRIORITY APPLN. INFO: GB 2002-13383 20020611
AN 2004-062228 [06] WPIDS
AB WO2003103717 A UPAB: 20040123
NOVELTY - A conjugate (C1) comprises a mitogen activated protein kinases kinase (MEK) **inhibitor** and a targeting agent.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for preparation of (C1) involving conjugating a MEK **inhibitor** to a targeting agent by hydrolyzable linker.
ACTIVITY - Antiarthritic; Cytostatic; Analgesic.
MECHANISM OF ACTION - Mitogen activated protein kinases kinase (MEK) **inhibitor.** Rats inducted with **inflammatory** **pain** were intraperitoneally injected with U0126

inhibitor (2 mg/kg) followed by administration of carrageenan after 30 minutes. The MEK activity was assessed by measuring the phosphorylation of extracellular regulated kinase (ERK)-1 using western blotting. The % change in pERK1 was found to be approx. 175 after 2 hours, which indicated an increase in MEK activity.

USE - In the manufacture of medicament for the **prevention**, **treatment** or amelioration of arthritis, cancer or chronic **pain** (e.g. neuropathic and **inflammatory pain**) (claimed).

ADVANTAGE - The targeting agent delivers the MEK **inhibitor** to sensory neurons, or neurons malfunctioning in neuropathic **pain** such as **C-fibers**, A **fibers** (preferably A delta fibres) or dorsal horn neurons. The MEK **inhibitor** is conjugated to the targeting agent by covalent linkage (e.g. ester, peptide or disulfide bond) that can be broken in vivo after the conjugate has been delivered to the cell and internalized.

Dwg.0/2

L20 ANSWER 7 OF 32 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2003400851 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12939335
TITLE: Early glial cell reactivity in experimental retinal detachment: effect of suramin.
AUTHOR: Uhlmann Susann; Bringmann Andreas; Uckermann Ortrud; Pannicke Thomas; Weick Michael; Ulbricht Elke; Goczalik Iwona; Reichenbach Andreas; Wiedemann Peter; Francke Mike
CORPORATE SOURCE: Department of Ophthalmology, Eye Clinic, University of Leipzig, Leipzig, Germany.
SOURCE: Investigative ophthalmology & visual science, (2003 Sep) Vol. 44, No. 9, pp. 4114-22.
Journal code: 7703701. ISSN: 0146-0404.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 27 Aug 2003
Last Updated on STN: 17 Sep 2003
Entered Medline: 16 Sep 2003

AB PURPOSE: In a rabbit model of retinal detachment, early Muller glial cell reactivity was monitored-specifically, changes in membrane features-to determine whether these changes involve an upregulation of purinergic P2 receptor-mediated responses and whether all or some of these alterations could be blocked by suramin or pyridoxal phosphate 6-azophenyl-2',4'-disulfonic acid (PPADS). In addition, the immune cell reactivity (microglial cells and blood-derived immune cells) was monitored. METHODS: A local retinal detachment was induced by subretinal injection of a sodium hyaluronate solution. Three, 24, 48, and 72 hours after surgery, Muller cells were acutely isolated, and patch-clamp records of the whole-cell potassium currents were made. The presence of P2 receptor-mediated responses was determined by measuring extracellular adenosine triphosphate (ATP)-induced membrane current increases, and by recording of ATP-induced calcium responses at the vitreal surface of retinal wholemounts. The density of **isolectin** B(4)-labeled immune cells was determined in the **nerve fiber** layer of retinal wholemounts. RESULTS: Within 24 hours of detachment, Muller cell reactivity was evident. The cells downregulated the density of their inwardly rectifying

potassium currents to 60% and 47% of the control value at 48 hours and 72 hours of detachment, respectively. This downregulation was accompanied by an enhanced incidence of cells which showed calcium and current responses after ATP application (control: 14%; 24 hours of detachment: 42%; 72 hours of detachment: 80%). Muller cell hypertrophy was apparent at 48 and 72 hours of detachment. Application of suramin during surgery **inhibited** the downregulation of potassium currents, but not the elevated responsiveness to extracellular ATP; PPADS had no effect. Suramin also **inhibited** the **inflammatory** response that was induced by the surgical procedure and that was apparent by the increased number of immune cells. CONCLUSIONS: Reactive responses of Muller cells occur within 24 hours of detachment. Suramin **inhibits** several (but not all) reactive glial alterations and therefore may represent one candidate for further investigations in the search for drugs that limit detrimental effects of immune cell activation and Muller cell gliosis during retinal detachment.

L20 ANSWER 8 OF 32 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2003167400 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12684478
TITLE: Resiniferatoxin induces paradoxical changes in thermal and mechanical sensitivities in rats: mechanism of action.
AUTHOR: Pan Hui-Lin; Khan Ghous M; Alloway Kevin D; Chen Shao-Rui
CORPORATE SOURCE: Department of Anesthesiology, The Pennsylvania State University College of Medicine, The Milton S. Hershey Medical Center, Hershey, Pennsylvania 17033-0850, USA.. hpan@psu.edu
CONTRACT NUMBER: GM64830 (NIGMS)
HL04199 (NHLBI)
NS41178 (NINDS)
SOURCE: The Journal of neuroscience : the official journal of the Society for Neuroscience, (2003 Apr 1) Vol. 23, No. 7, pp. 2911-9.
Journal code: 8102140. E-ISSN: 1529-2401.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 16 Apr 2003
Last Updated on STN: 31 May 2003
Entered Medline: 30 May 2003

AB Resiniferatoxin (RTX), an ultrapotent analog of capsaicin, has been used as a tool to study the role of capsaicin-sensitive **C fibers** in **pain.** Recently, we found that RTX diminished the thermal sensitivity but unexpectedly increased the sensitivity to tactile stimulation in adult rats. In this study, we explored the potential mechanisms involved in RTX-induced changes in somatosensory function. An intraperitoneal injection of 200 microg/kg RTX, but not its vehicle, rapidly produced an increase in the paw withdrawal latency to a heat stimulus. Also, profound tactile allodynia developed in all the RTX-**treated** rats in 3 weeks. This paradoxical change in thermal and mechanical sensitivities lasted for at least 6 weeks. Electron microscopic examination of the sciatic nerve revealed a loss of unmyelinated fibers and extensive ultrastructural damage of myelinated fibers in RTX-**treated** rats. Immunofluorescence labeling showed a diminished vanilloid

receptor 1 immunoreactivity in dorsal root ganglia neurons and the spinal dorsal horn of RTX-**treated** rats. Furthermore, two transganglionic tracers, horseradish peroxidase conjugates of cholera toxin B subunit (CTB) and **isolectin**-B(4) of Bandeiraea simplicifolia (IB(4)), were injected into the opposite sides of the sciatic nerve to trace myelinated and unmyelinated afferent terminations, respectively, in the spinal dorsal horn. In RTX-**treated** rats, IB(4)-labeled terminals in the dorsal horn were significantly reduced, and CTB-labeled terminals appeared to sprout into lamina II of the spinal dorsal horn. Thus, this study demonstrates that systemic RTX diminishes the thermal **pain** sensitivity by depletion of unmyelinated afferent neurons. The delayed tactile allodynia induced by RTX is likely attributable to damage to myelinated afferent fibers and their abnormal sprouting in lamina II of the spinal dorsal horn. These data provide new insights into the potential mechanisms of postherpetic neuralgia.

L20 ANSWER 9 OF 32 EMBASE

ACCESSION NUMBER: 2003266054 EMBASE
TITLE: Expression of oncostatin M receptor β in a specific subset of nociceptive sensory neurons.
AUTHOR: Tamura S.; Morikawa Y.; Miyajima A.; Senba E.
CORPORATE SOURCE: Dr. Y. Morikawa, Dept. of Anatomy and Neurobiology, Wakayama Medical University, 811-1 Kimiidera, Wakayama, 641-8509, Japan. yoshim@wakayama-med.ac.jp
SOURCE: European Journal of Neuroscience, (2003) Vol. 17, No. 11, pp. 2287-2298. .
Refs: 53
ISSN: 0953-816X CODEN: EJONEI
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 24 Jul 2003
Last Updated on STN: 24 Jul 2003

AB Oncostatin M belongs to the interleukin-6 family of cytokines and acts as a multifunctional cytokine during murine embryogenesis and in **inflammatory** reactions. Although it has been demonstrated that oncostatin M has biological activities on many types of cells, including hepatocytes, dermal fibroblasts and endothelial cells, the roles of oncostatin M in the murine peripheral nervous system remain unclear. Here, we investigated the expression of specific β-subunit of oncostatin M receptor in the dorsal root ganglia of adult mice. In the adult dorsal root ganglia, β-subunit of oncostatin M receptor was exclusively expressed in small-sized neurons. Approximately 13% of total dorsal root ganglia neurons in mice contained β-subunit of oncostatin M receptor. The double-immunofluorescence method revealed that approximately 28% of β-subunit of oncostatin M receptor-positive neurons contained TrkA immunoreactivity, 63% expressed Ret immunoreactivity and 58% bound **isolectin** B4. No neuropeptides, including substance P and calcitonin gene-related peptide, were contained in the neurons. In addition, all β-subunit of oncostatin M receptor-positive neurons expressed both vanilloid receptor 1 and P2X3 purinergic receptor. These neurons projected to the inner portion of lamina II in the dorsal horn of spinal cord and the dermis of skin. Seven days after sciatic nerve axotomy, the expression of β-subunit of

oncostatin M receptor was down-regulated in the lumbar dorsal root ganglia of the injured side. Our study demonstrated that β-subunit of oncostatin M receptor was expressed in both cell bodies and processes of nonpeptidergic nociceptive neurons in adult mice, suggesting that oncostatin M may affect the nociceptive function of the neurons through the **modulation** of vanilloid receptor 1 and P2X3 expression.

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ACCESSION NUMBER: 2003423716 EMBASE
TITLE: Targeted toxins in **pain.**
AUTHOR: Wiley R.G.; Lappi D.A.
CORPORATE SOURCE: R.G. Wiley, VAMC, Neurology Service 127, 1310 24th Avenue South, Nashville, TN 37212-2637, United States. ronald.g.wiley@vanderbilt.edu
SOURCE: Advanced Drug Delivery Reviews, (15 Aug 2003) Vol. 55, No. 8, pp. 1043-1054. .
Refs: 96
ISSN: 0169-409X CODEN: ADDREP
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 6 Nov 2003
Last Updated on STN: 6 Nov 2003

AB Although only recently applied to the study of nociception, 'molecular neurosurgery', producing highly selective neural lesions using targeted cytotoxins, has proven a valuable tool for analysis of nociceptive systems and promises to yield much more information on the role of specific types of neurons in **pain** perception and possibly new **pain therapies.** Neuropeptide-toxin conjugates, particularly, substance P-saporin, have proven useful research tools and may find clinical applications. Targeting non-lethal moieties (enzymes, genes, viruses) also may prove useful for research and **therapeutic** purposes.

L20 ANSWER 11 OF 32 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER: 2003504435 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14580941
TITLE: Distribution of antinociceptive adenosine A1 receptors in the spinal cord dorsal horn, and relationship to primary afferents and neuronal subpopulations.
AUTHOR: Schulte G; Robertson B; Fredholm B B; DeLander G E; Shortland P; Molander C
CORPORATE SOURCE: Department of Physiology and Pharmacology, Karolinska Institutet, SE-171 77 Stockholm, Sweden.. gunnar.schulte@mbb.ki.se
SOURCE: Neuroscience, (2003) Vol. 121, No. 4, pp. 907-16.
Journal code: 7605074. ISSN: 0306-4522.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403

Searcher : Shears 571-272-2528

ENTRY DATE: Entered STN: 29 Oct 2003
Last Updated on STN: 2 Mar 2004
Entered Medline: 1 Mar 2004

AB Adenosine can reduce **pain** and allodynia in animals and man, probably via spinal adenosine A1 receptors. In the present study, we investigate the distribution of the adenosine A1 receptor in the rat spinal cord dorsal horn using immunohistochemistry, in situ hybridization, radioligand binding, and confocal microscopy. In the lumbar cord dorsal horn, dense immunoreactivity was seen in the inner part of lamina II. This was unaltered by dorsal root section or thoracic cord hemisection. Confocal microscopy of the dorsal horn revealed close anatomical relationships but no or only minor overlap between A1 receptors and immunoreactivity for markers associated with primary afferent central endings: calcitonin gene-related peptide, or **isolectin** B4, or with neuronal subpopulations: mu-opioid receptor, neuronal nitric oxide synthase, met-enkephalin, parvalbumin, or protein kinase Cgamma, or with glial cells: glial fibrillary acidic protein. A few adenosine A1 receptor positive structures were double-labeled with alpha-amino-3-hydroxy-5-methyl-4-isoaxolepropionic acid glutamate receptor subunits 1 and 2/3. The results indicate that most of the adenosine A1 receptors in the dorsal horn are located in inner lamina II postsynaptic neuronal cell bodies and processes whose functional and neurochemical identity is so far unknown. Many adenosine A1 receptor positive structures are in close contact with **isolectin** B4 positive **C-fiber** primary afferents and/or postsynaptic structures containing components of importance for the **modulation** of nociceptive information.

L20 ANSWER 12 OF 32 EMBASE

ACCESSION NUMBER: 2004068498 EMBASE
TITLE: The effect of **treatment** with BRX-220, a co-inducer of heat shock proteins, on sensory fibers of the rat following peripheral nerve injury.
AUTHOR: Kalmar B.; Greensmith L.; Malcangio M.; McMahon S.B.; Csermely P.; Burnstock G.
CORPORATE SOURCE: B. Kalmar, Sobell Dept. Motor Neurosci. M., Institute of Neurology, Queen Square, London WC1N 3BG, United Kingdom. b.kalmar@ucl.ac.uk
SOURCE: Experimental Neurology, (2003) Vol. 184, No. 2, pp. 636-647. .
Refs: 33
ISSN: 0014-4886 CODEN: EXNEAC
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 4 Mar 2004
Last Updated on STN: 4 Mar 2004

AB In this study, we examined the effect BRX-220, a co-inducer of heat shock proteins, in injury-induced peripheral neuropathy. Following sciatic nerve injury in adult rats and **treatment** with BRX-220, the following features of the sensory system were studied: (a) expression of calcitonin gene-related peptide (CGRP); (b) binding of **isolectin** B4 (IB4) in dorsal root ganglia (DRG) and spinal cord; (c) stimulation-evoked release of substance P (SP) in an in vitro spinal cord preparation and (d) nociceptive responses of

partially denervated rats. BRX-220 partially reverses axotomy-induced changes in the sensory system. In vehicle-**treated** rats there is a decrease in IB4 binding and CGRP expression in injured neurones, while in BRX-220-**treated** rats these markers were better preserved. Thus, 7.0 ± 0.6% of injured DRG neurones bound IB4 in vehicle-**treated** rats compared to 14.4 ± 0.9% in BRX-220-**treated** animals. Similarly, 4.5 ± 0.5% of DRG neurones expressed CGRP in the vehicle-**treated** group, whereas 9.0 ± 0.3% were positive in the BRX-220-**treated** group. BRX-220 also partially restored SP release from spinal cord sections to electrical stimulation of primary sensory neurones. Behavioural tests carried out on partially denervated animals showed that BRX-220 **treatment** did not **prevent** the emergence of mechanical or thermal hyperalgesia. However, oral **treatment** for 4 weeks lead to reduced **pain**-related behaviour suggesting either slowly developing analgesic actions or enhancement of recovery processes. Thus, the morphological improvement seen in sensory neurone markers was accompanied by restored functional activity. Therefore, **treatment** with BRX-220 promotes restoration of morphological and functional properties in the sensory system following peripheral nerve injury.

L20 ANSWER 13 OF 32 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:160650 BIOSIS
DOCUMENT NUMBER: PREV200400160800
TITLE: Knee joint injection with a single dose of capsaicin depletes small peripheral nerves and ameliorates **inflammatory** severity in rats with CFA arthritis.
AUTHOR(S): Zhang, L. P. [Reprint Author]; Roozen, P. M. [Reprint Author]; Westlund, K. N. [Reprint Author]
CORPORATE SOURCE: Dept. Anatom. and Neurosci, Univ. Texas, Med. Br., Galveston, TX, USA
SOURCE: Society for Neuroscience Abstract Viewer and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. 66.9. http://sfn.scholarone.com. e-file.
Meeting Info.: 33rd Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 08-12, 2003. Society of Neuroscience.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Mar 2004
Last Updated on STN: 24 Mar 2004

AB This study investigated the effects of selectively depleting small **nerve fibers** with capsaicin, on knee joint **inflammation** in an experimental monoarthritis rat model. Monoarthritis was induced by injection of complete Freund's adjuvant (CFA, 0.1ml) into one knee joint. Capsaicin (1%, 0.1ml) or vehicle was injected one day after CFA injection. Knee joint **inflammation** was assessed by measuring knee joint diameter and cutaneous temperature. Secondary hyperalgesia was assessed with thermal paw withdrawal latency (PWL) testing. Seven days after CFA injection, rats were perfused and knee joints, lumbar dorsal root ganglia (DRG) and lumbar spinal cord were harvested. Immunofluorescent staining was used to identify the presence and abundance of small fibers using antibody specific for neurotransmitter calcitonin gene-related peptide (CGRP) and the non-peptide containing

small fiber binding protein, **isolectin** B4 (IB(4)). Large fibers were identified using anti-neurofilament protein (NFP 200).Results showed an increase in CGRP and IB(4) immunostaining in synovial membrane of inflamed knee joints and a decrease in lumbar spinal cord seven days after CFA injection. A single dose of capsaicin injected into knee joint depleted small fiber terminals (large fibers remained) in knee joint synovial membrane in control and arthritis rats. Furthermore, capsaicin **treatment** significantly improved knee joint **inflammation**, including restoration of PWL and knee joint diameter to baseline. This decrease in neurotransmitters in spinal cord was reversed in CFA arthritis rats. These results suggest that selective destruction of small sensory fibers in the knee joint with capsaicin substantially reduces the outcome of chronic peripheral **inflammation** induced by CFA.

L20 ANSWER 14 OF 32 MEDLINE on STN
ACCESSION NUMBER: 2002258062 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11997700
TITLE: Trichloroethanol alters action potentials in a subgroup of primary sensory neurones.
AUTHOR: Gruss Marco; Hempelmann Gunter; Scholz Andreas
CORPORATE SOURCE: Physiologisches Institut, Justus-Liebig-Universitat, 35385 Giessen, Germany.
SOURCE: Neuroreport, (2002 May 7) Vol. 13, No. 6, pp. 853-6. Journal code: 9100935. ISSN: 0959-4965.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 9 May 2002
Last Updated on STN: 27 Jun 2002
Entered Medline: 26 Jun 2002

AB We investigated the effects of 2,2,2-trichloroethanol (TCE), the active metabolite of chloral hydrate, on large-conductance calcium-activated K+ channels (BKCa channels) of dorsal root ganglion (DRG) neurones. In outside-out patches, 2 and 5 mM TCE increased the open probability of BKCa channels to 1.7-fold and 2.8-fold of control, respectively. In 50% of the cells investigated (group A) the action potential (AP) was shortened reversibly by TCE by 20% and the whole-cell outward-current was increased by 44%. Both effects could be antagonized by iberiotoxin. In a second group of neurone (group B), TCE prolonged the AP duration. The effects of TCE in group A, which was 20-fold more potent than ethanol on BKCa channels and AP might contribute to the described analgesic effect of chloral hydrate.

L20 ANSWER 15 OF 32 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2002378710 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12123694
TITLE: Origins of skeletal **pain**: sensory and sympathetic innervation of the mouse femur.
AUTHOR: Mach D B; Rogers S D; Sabino M C; Luger N M; Schwei M J; Pomonis J D; Keyser C P; Clohisy D R; Adams D J; O'Leary P; Mantyh P W
CORPORATE SOURCE: Neurosystems Center, University of Minnesota, 18-208 Moos Tower, 515 Delaware Street S.E., Minneapolis, MN 55455, USA.
CONTRACT NUMBER: AR 43595 (NIAMS)
DE 00270 (NIDCR)

DE 07288 (NIDCR)
NIDA 11986 (NIDA)
NS 23970 (NINDS)
SOURCE: Neuroscience, (2002) Vol. 113, No. 1, pp. 155-66.
Journal code: 7605074. ISSN: 0306-4522.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 19 Jul 2002
Last Updated on STN: 17 Oct 2002
Entered Medline: 16 Oct 2002

AB Although skeletal **pain** plays a major role in reducing the quality of life in patients suffering from osteoarthritis, Paget's disease, sickle cell anemia and bone cancer, little is known about the mechanisms that generate and maintain this **pain.** To define the peripheral fibers involved in transmitting and **modulating** skeletal **pain**, we used immunohistochemistry with antigen retrieval, confocal microscopy and three-dimensional image reconstruction of the bone to examine the sensory and sympathetic innervation of mineralized bone, bone marrow and periosteum of the normal mouse femur. Thinly myelinated and unmyelinated peptidergic sensory fibers were labeled with antibodies raised against calcitonin gene-related peptide (CGRP) and the unmyelinated, non-peptidergic sensory fibers were labeled with the **isolectin** B4 (Bandeira simplicifolia). Myelinated sensory fibers were labeled with an antibody raised against 200-kDa neurofilament H (clone RT-97). Sympathetic fibers were labeled with an antibody raised against tyrosine hydroxylase. CGRP, RT-97, and tyrosine hydroxylase immunoreactive fibers, but not **isolectin** B4 positive fibers, were present throughout the bone marrow, mineralized bone and the periosteum. While the periosteum is the most densely innervated tissue, when the total volume of each tissue is considered, the bone marrow receives the greatest total number of sensory and sympathetic fibers followed by mineralized bone and then periosteum.Understanding the sensory and sympathetic innervation of bone should provide a better understanding of the mechanisms that drive bone **pain** and aid in developing **therapeutic** strategies for **treating** skeletal **pain.**

L20 ANSWER 16 OF 32 EMBASE

ACCESSION NUMBER: 2002253961 EMBASE
TITLE: Priming by muscle **inflammation** alters the response and vulnerability to axotomy-induced damage of the rat facial motor nucleus.
AUTHOR: Mariotti R.; Tongiorgi E.; Bressan C.; Kristensson K.; Bentivoglio M.
CORPORATE SOURCE: R. Mariotti, Department of Morphological Science, University of Verona, 37134 Verona, Italy
SOURCE: Experimental Neurology, (2002) Vol. 176, No. 1, pp. 133-142. .
Refs: 23
ISSN: 0014-4886 CODEN: EXNEAC
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
LANGUAGE: English

SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 25 Jul 2002
Last Updated on STN: 25 Jul 2002

AB To ascertain whether signaling due to peripheral **inflammation** affects motoneuron vulnerability, we examined in adult rats the reaction to axonal injury of facial motoneurons primed by muscle **inflammation.** In this double-hit paradigm, preconditioning was achieved by injections into the facial muscles of the T cell mitogen phytohemagglutinin, which was found in a previous study (11) to elicit a retrograde response in motoneurons. Facial nerve transection was used as test lesion. Intramuscular injections of saline prior to axotomy were used as control for **lectin** pretreatment. In rats pretreated with phytohemagglutinin injection, upregulation of the expression of the antiapoptotic bcl-2 gene, examined with in situ hybridization, was significantly higher in facial motoneurons at 2 days postaxotomy compared with saline-injected control cases. After repeated phytohemagglutinin injections followed by nerve transection, induction in facial motoneurons of nitric oxide synthase, revealed by histochemistry and immunohistochemistry, as well as activation of the surrounding microglia, was enhanced at 14 days postaxotomy with respect to the saline-**treated** control cases. At the same time point, no significant intergroup difference was detected in the intensity of astrocytic activation. At 1 month postaxotomy, stereological cell counts revealed that motoneuron loss was significantly greater in the cases pretreated with phytohemagglutinin than in the saline-**treated** cases. The data point out that the response of the facial motor nucleus to axonal damage is altered by previous exposure to peripheral **inflammation** and that such preconditioning stimulus enhances motoneuron vulnerability to nerve injury. .COPYRGT. 2002 Elsevier Science (USA).

L20 ANSWER 17 OF 32 MEDLINE on STN
ACCESSION NUMBER: 2002295939 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12012376
TITLE: Stereological analysis of Ca(2+)/calmodulin-dependent protein kinase II alpha -containing dorsal root ganglion neurons in the rat: colocalization with **isolectin** Griffonia simplicifolia, calcitonin gene-related peptide, or vanilloid receptor 1.
AUTHOR: Carlton Susan M; Hargett Gregory L
CORPORATE SOURCE: Department of Anatomy and Neurosciences, Marine Biomedical Institute, University of Texas Medical Branch, Galveston, Texas 77555-1069, USA.. smcarlto@utmb.edu
CONTRACT NUMBER: NS11255 (NINDS)
NS27910 (NINDS)
NS40700 (NINDS)
SOURCE: The Journal of comparative neurology, (2002 Jun 17) Vol. 448, No. 1, pp. 102-10.
Journal code: 0406041. ISSN: 0021-9967.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 31 May 2002
Last Updated on STN: 13 Jul 2002
Entered Medline: 12 Jul 2002

AB The enzyme Ca(2+)/calmodulin-dependent protein kinase II (CaMKII) is

widely distributed in the nervous system. A previous report describes immunostaining for CaMKII alpha in dorsal root ganglion (DRG) neurons. In this study, CaMKII alpha is colocalized in the rat with three putative markers of nociceptive DRG neurons, **isolectin** Griffonia simplicifolia (I-B4), identifying small-diameter, "peptide-poor" neurons; calcitonin gene-related peptide (CGRP), identifying " peptide-rich" neurons; or the vanilloid receptor 1 (VR1), identifying neurons activated by heat, acid, and capsaicin. Lumbar 4 and 5 DRG sections were labeled using immunofluorescence or **lectin** binding histochemistry, and percentages of single and double-labeled CaMKIIalpha neurons were determined. Stereological estimates of total neuron number in the L4 DRG were 13,815 +/- 2,798 and in the L5 DRG were 14,111 +/- 4,043. Percentages of single-labeled L4 DRG neurons were 41% +/- 2% CaMKII alpha, 38% +/- 3% I-B4, 44% +/- 3% CGRP, and 32% +/- 6% VR1. Percentages of single-labeled L5 DRG neurons were 44% +/- 5% CaMKII alpha, 48% +/- 2% I-B4, 41% +/- 7% CGRP, and 39% +/- 14% VR1. For L4 and L5, respectively, estimates of double-labeled CaMKII alpha neurons showed 34% +/- 2% and 38% +/- 17% labeled for I-B4, 25% +/- 14% and 19% +/- 10% labeled for CGRP, and 37% +/- 7% and 38% +/- 5% labeled for VR1. Conversely, for L4 and L5, respectively, 39% +/- 14% and 38% +/- 7% I-B4 binding neurons, 24% +/- 12% and 23% +/- 10% CGRP neurons, and 42% +/- 7% and 35% +/- 7% VR1 neurons labeled for CaMKIIalpha. The mean diameter of CaMKII alpha - labeled neurons was approximately 27 microm, confirming that this enzyme was preferentially localized in small DRG neurons. The results indicate that subpopulations of DRG neurons containing CaMKII alpha are likely to be involved in the processing of nociceptive information. Thus, this enzyme may play a critical role in the **modulation** of nociceptor activity and plasticity of primary sensory neurons.

L20 ANSWER 18 OF 32 MEDLINE on STN
ACCESSION NUMBER: 2001650646 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11703454
TITLE: Ethanol reduces excitability in a subgroup of primary sensory neurons by activation of BK(Ca) channels.
AUTHOR: Gruss M; Henrich M; Konig P; Hempelmann G; Vogel W; Scholz A
CORPORATE SOURCE: Physiologisches Institut, Justus-Liebig-Universitat, 35385 Giessen, Germany.
SOURCE: The European journal of neuroscience, (2001 Oct) Vol. 14, No. 8, pp. 1246-56.
Journal code: 8918110. ISSN: 0953-816X.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 13 Nov 2001
Last Updated on STN: 23 Jan 2002
Entered Medline: 18 Dec 2001

AB Ethanol effects on the central nervous system have been well investigated and described in recent years; **modulations**, by ethanol, of several ligand-gated and voltage-gated ion channels have been found. In this paper, we describe a shortening of action potential duration (APD) by ethanol in approximately equal to 40% of small diameter neurons in rat dorsal root ganglia (DRG). In these neurons, designated as group A neurons, we observed an ethanol-induced increase in whole-cell outward-current. As iberiotoxin, a specific

blocker of large-conductance calcium-activated K+ channels (BK(Ca) channels), blocks the effects of ethanol, we investigated the interaction between these channels and ethanol in outside-out patches. Open probability of BK(Ca) channels was increased 2-6 x depending on the concentration (40-80 mM approximately equal to 2-4 per thousand v/v) of ethanol. Functional consequences were a prolongation of the refractory period, which was reversible after addition of iberiotoxin, and reduced firing frequency during ethanol application. In contrast, another type of neuron (group B) showed a prolonged APD during application of ethanol which was irreversible in most cases. In 90% of cases, neurons of group A showed a positive staining for **isolectin** B4 (I-B4), a marker for nociceptive neurons. We suggest that the activation of BK(Ca) channels induced by clinically relevant concentrations of ethanol, the resulting **modulations** of APD and refractory period of DRG neurons, might contribute to clinically well-known ethanol-induced analgesia and paresthesia.

L20 ANSWER 19 OF 32 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 5

ACCESSION NUMBER: 2001:498681 BIOSIS
DOCUMENT NUMBER: PREV200100498681
TITLE: Localization of metabotropic glutamate receptors 2/3 on primary afferent axons in the rat.
AUTHOR(S): Carlton, S. M. [Reprint author]; Hargett, G. L.; Coggeshall, R. E.
CORPORATE SOURCE: Department of Anatomy and Neurosciences, Marine Biomedical Institute, University of Texas Medical Branch, 301 University Boulevard, Galveston, TX, 77555-1069, USA
smcarlto@utmb.edu
SOURCE: Neuroscience, (22 August, 2001) Vol. 105, No. 4, pp. 957-969. print.
CODEN: NRSCDN. ISSN: 0306-4522.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Oct 2001
Last Updated on STN: 23 Feb 2002

AB The goal of the present study is to determine the relationship of metabotropic glutamate receptors 2/3 (mGluR2/3) to dorsal root ganglion cells, peripheral primary afferent **fibers** in digital **nerves** and central primary afferent fibers in the spinal cord. We demonstrate that approximately 40% of L4 and L5 dorsal root ganglion cells contain mGluR2/3-like immunoreactivity. These mGluR2/3-positive cells are small in diameter (23 mum) and 76% stain for the **isolectin** Griffonia simplicifolia (I-B4), while 67% of I-B4 cells have mGluR2/3-like immunoreactivity. Electron microscopic analyses of mGluR2/3-like immunoreactivity in axons in digital nerves indicate that 32% of unmyelinated and 28% of myelinated axons are labeled. In the lumbar dorsal horn, mGluR2/3-like immunoreactivity is localized preferentially in lamina IIi with lighter staining in laminae III and IV. The dense mGluR2/3-like immunoreactivity in lamina IIi is consistent with the localization of these receptors in I-B4-labeled dorsal root ganglion cells. Elimination of primary afferent input following unilateral dorsal rhizotomies significantly decreases the mGluR2/3-like immunoreactivity density in the dorsal horn although some residual staining does remain, suggesting that many but not all of these receptors are located on primary afferent processes. The finding that mGluR2/3s are located on peripheral sensory axons suggests that they are involved in peripheral sensory transduction and can **modulate**

transmission of sensory input before it reaches the spinal cord. This offers the possibility of altering sensory input, particularly noxious input, at a site that would avoid CNS side effects. Since many but not all of these receptors are located on primary afferent terminals, these receptors may also influence primary afferent transmission in the dorsal horn through presynaptic mechanisms and glutamatergic transmission in general through both presynaptic and postsynaptic mechanisms. Since these receptors are concentrated in lamina IIi and also largely co-localized with I-B4, they may have considerable influence on nociceptive processing by what are considered to be non-peptidergic primary afferent neurons.

L20 ANSWER 20 OF 32 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2001675268 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11720789
TITLE: The expression of bradykinin B(1) receptors on primary sensory neurones that give rise to small caliber sciatic **nerve fibres** in rats.
AUTHOR: Ma Q P
CORPORATE SOURCE: Department of Pharmacology, Merck Sharp & Dohme Research Laboratories, Neuroscience Research Centre, Terlings Park, Harlow CM20 2QR, UK.. qingping_ma@merck.com
SOURCE: Neuroscience, (2001) Vol. 107, No. 4, pp. 665-73. Journal code: 7605074. ISSN: 0306-4522.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 27 Nov 2001
Last Updated on STN: 7 Mar 2002
Entered Medline: 5 Mar 2002

AB The bradykinin B(1) receptor has been considered as an important mediator for **inflammatory pain.** In the present study, we have investigated the **fibre** types of sciatic **nerve** primary sensory neurones that express B(1) receptors by retrograde tracing in combination with immunohistochemical staining, or double-immunohistochemical staining. Approximately 12% of the A-fibre dorsal root ganglion neurones, retrogradely labelled from an intra-sciatic nerve injection of fluorescein isothiocyanate-conjugated cholera toxin B subunit, were B(1) receptor-immunoreactive. Over 70% of the small diameter dorsal root ganglion neurones, retrogradely labelled from an intra-sciatic nerve injection of tetramethylrhodamine isothiocyanate-conjugated wheat germ agglutinin, were B(1) receptor-immunoreactive. Over 50% of the (predominantly non-peptidergic) **C-fibre** dorsal root ganglion neurones, retrogradely labelled from an intra-sciatic nerve injection of fluorescein isothiocyanate-conjugated Bandeiraea simplicifolia **isolectin** B4, were B(1) receptor-immunoreactive. When calcitonin gene-related peptide, which is contained mainly in small caliber **C**- and A(delta)-**fibre** primary afferents, and B(1) receptors were stained with a double-immunofluorescent method, over 80% of the calcitonin gene-related peptide-positive dorsal root ganglion neurones were B(1) receptor-immunoreactive.From these results we suggest that B(1) receptors are predominantly expressed by small diameter primary afferent neurones that give rise to sciatic **nerve fibres**, which include both peptidergic and non-peptidergic **C-fibres** and A(delta)-fibres. Since peripheral nociceptive information is

primarily transmitted by **C**- and A(delta)-**fibres**, B(1) receptors may be involved in the **modulation** of nociceptive transduction or transmission.

L20 ANSWER 21 OF 32 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2001191989 EMBASE
TITLE: ATP affects both axons and Schwann cells of unmyelinated **C fibres.**
AUTHOR: Irnich D.; Burgstahler R.; Bostock H.; Grafe P.
CORPORATE SOURCE: P. Grafe, Department of Physiology, University of Munich, D-80336 Munich, Germany. p.grafe@lrz.uni-muenchen.de
SOURCE: Pain, (2001) Vol. 92, No. 3, pp. 343-350. .
Refs: 30
ISSN: 0304-3959 CODEN: PAINDB
PUBLISHER IDENT.: S 0304-3959(01)00277-9
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 14 Jun 2001
Last Updated on STN: 14 Jun 2001

AB Recent studies indicate that effects of ATP on unmyelinated afferent **nerve fibres** contribute to the transduction of nociceptive and non-nociceptive stimuli. In the present study, effects of ATP were studied on axons and Schwann cells of **C fibres** in isolated rat vagus nerves. A combination of a computerised threshold tracking technique with photometric and confocal measurements of the free intracellular Ca(2+) concentration revealed differences in the effect of ATP and related compounds. Pyridoxal-phosphate-6-azophenyl-2',5'-disulphonic acid (iso-PPADS, an antagonist of ionotropic P2X receptors) completely blocked the excitatory effect of α,β-meATP on unmyelinated axons, whereas the effects of ATP and 2-Cl-ATP were only slightly changed. Moreover, the threshold lowering effects of ATP and 2-Cl-ATP, but not of α,β-meATP, were accompanied by intracellular Ca(2+) transients. In confocal imaging experiments, the **lectin** IB4 was used to identify unmyelinated **nerve fibres** and their ensheathing Schwann cells. The Schwann cells were identified as the cellular elements underlying ATP-induced Ca(2+) transients. In addition, an increase in axonal excitability of **C fibres** was seen during a rise in [Ca(2+)](i) induced by **inhibition** of the endoplasmic Ca(2+) ATPase with cyclopiazonic acid. These data show that an increase of the extracellular ATP concentration in an intact peripheral nerve trunk activates both axons and Schwann cells. It appears that P2 nucleotide receptors on Schwann cells may contribute to the excitatory effect of ATP observed on unmyelinated, including nociceptive, axons. .COPYRGT. 2001 Elsevier Science B.V.

L20 ANSWER 22 OF 32 MEDLINE on STN DUPLICATE 7

ACCESSION NUMBER: 2001130385 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11113318
TITLE: Localization of N-methyl-D-aspartate NR2B subunits on primary sensory neurons that give rise to small-caliber sciatic **nerve fibers** in rats.
AUTHOR: Ma Q P; Hargreaves R J
CORPORATE SOURCE: Department of Pharmacology, Merck Sharp & Dohme

Research Laboratories, Neuroscience Research Centre, Terlings Park, CM20 2QR, Harlow, UK..
qingping_ma@merck.com
SOURCE: Neuroscience, (2000) Vol. 101, No. 3, pp. 699-707.
Journal code: 7605074. ISSN: 0306-4522.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 4 Apr 2001
Last Updated on STN: 4 Apr 2001
Entered Medline: 1 Mar 2001

AB In the present study we have used immunohistochemical staining and retrograde tracing techniques to investigate the relationship between the N-methyl-D-aspartate receptor NR2B subunits and small-diameter primary afferent dorsal root ganglion neurons that give rise to the sciatic **nerve fibers.** Three days after an intra-sciatic nerve injection of tetramethyl rhodamine isothiocyanate-conjugated wheat germ agglutinin which labels small-diameter primary afferents, many NR2B and wheat germ agglutinin-double-labeled cells (approximately 70% of wheat germ agglutinin-labeled neurons) were observed in the L5 dorsal root ganglia. Three days after an intra-sciatic nerve injection of fluorescein isothiocyanate-conjugated Bandeiraea simplicifolia agglutinin **isolectin** B4 which labels predominantly non-peptidergic **C-fiber** primary afferents, NR2B and Bandeiraea simplicifolia agglutinin **isolectin** B4 double-labeled neurons (approximately 90% of Bandeiraea simplicifolia agglutinin **isolectin** B4-labeled neurons) were also observed in the L5 dorsal root ganglion. Three days after an intra-sciatic nerve injection of fluorescein isothiocyanate-conjugated cholera toxin B subunit, only approximately 40% of cholera toxin B subunit-labeled neurons were NR2B positive and those labeled neurons tended to be small-sized. When calcitonin gene-related peptide and NR2B were labeled by a double immunofluorescent staining technique, we found that the majority of calcitonin gene-related peptide-positive neurons was NR2B immunoreactive (>90% of calcitonin gene-related peptide-positive neurons, and approximately 60% of NR2B-positive neurons) as well. Size frequency analysis also demonstrated that NR2B subunits were predominantly localized on the small and medium-sized neurons.These results suggest that NR2B subunits are predominantly expressed on small diameter primary afferents, and these NR2B containing N-methyl-D-aspartate receptors may play a role in the **modulation** of neurotransmitter release from primary afferent terminals.

L20 ANSWER 23 OF 32 EMBASE
ACCESSION NUMBER: 2000400189 EMBASE
TITLE: Neuronal lesioning with axonally transported toxins.
AUTHOR: Wiley R.G.; Kline IV R.H.
CORPORATE SOURCE: R.G. Wiley, Neurology Service (127), VAMC, 1310 24th Avenue, South, Nashville, TN 37212-2637, United States.
ronald.g.wiley@vanderbilt.edu
SOURCE: Journal of Neuroscience Methods, (15 Nov 2000) Vol. 103, No. 1, pp. 73-82. .
Refs: 115
ISSN: 0165-0270 CODEN: JNMEDT
PUBLISHER IDENT.: S 0165-0270(00)00297-1

COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 2000
Last Updated on STN: 13 Dec 2000

AB Axonally transported toxins can be used to make selective lesions of the nervous system. Collectively, these techniques are termed 'molecular neurosurgery' because they exploit the surface molecular identity of neurons to selectively destroy specific types of neurons. Suicide transport, is anatomically selective but not type-selective. The most widely used suicide transport agents are the toxic **lectins** (ricin, volkensin) and the immunotoxin, OX7-saporin. The toxic **lectins** and saporin are ribosome inactivating proteins that irreversibly **inhibit** protein synthesis. The toxic **lectins** have binding subunits but saporin requires a targeting vector to gain entrance into cells. Immunolesioning uses monoclonal anti-neuronal antibodies to deliver saporin selectively into neurons that express a particular target surface antigen. Neuropeptide-saporin conjugates selectively destroy neurons expressing the appropriate peptide receptors. Notable experimental uses of these agents include analysis of the function of the cholinergic basal forebrain (192-saporin) and **pain** research (anti-DBH-saporin, substance P-saporin). It is likely that more immunolesioning and neuropeptide-toxin conjugates will be developed in the near future. (C) 2000 Published by Elsevier Science B.V.

L20 ANSWER 24 OF 32 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:134346 BIOSIS
DOCUMENT NUMBER: PREV200100134346
TITLE: Sensory nerves that innervate bone are involved in conveying skeletal **pain.**
AUTHOR(S): Mach, D. B. [Reprint author]; Rogers, S. D.; Kotz, C. M.; Clohisy, D. R.; Mantyh, P. W.
CORPORATE SOURCE: U of MN, Minneapolis, MN, USA
SOURCE: Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-734.1. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 04-09, 2000. Society for Neuroscience.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Mar 2001
Last Updated on STN: 15 Feb 2002

AB **Pain** arising from bone, whether it is due to bone cancer, osteoporosis, fracture or other diseases that involve the skeleton can be intense and difficult to **treat.** In an attempt to better understand the location and phenotype of sensory nerves that transmit **pain** arising from bone, we have defined the sensory innervation of the mouse femur. Unmyelinated sensory fibers were labeled with the **isolectin** IB4, and anti-CGRP and myelinated **nerve fibers** with anti-RT-97. Whereas, the periosteum received a rich innervation of both CGRP and RT-97 expressing fibers, few IB4 positive fibers were present. Surprisingly, mineralized bone also received a rich innervation of both CGRP and RT-97 positive fibers (again, few IB4 positive fibers

were observed) with the density of sensory innovation showing a correlation with metabolic activity of the bone. Thus, the shaft of the femur received a sparse sensory innervation whereas the proximal and distal heads of the femur were richly innervated. Within mineralized bone, the CGRP and RT-97 positive fibers were present within the Haversian canals of mineralized bone and associated with blood vessels in marrow and spongy bone. These findings suggest a much richer innervation of mineralized bone, spongy bone and marrow than has previously been generally appreciated. This extensive sensory innervation suggests that **pain** in pathological conditions such as bone cancer, osteoporosis, or fractures could arise from sensory fibers that innervate these intraosseous structures as well as mechanical distortion of the periosteum. Determining the factors that stimulate the receptors and channels expressed by these sensory fibers that innervate bone may lead to a new understanding of skeletal **pain** and **therapies** for its **treatment.**

L20 ANSWER 25 OF 32 MEDLINE on STN
ACCESSION NUMBER: 1999268601 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10338279
TITLE: Purification of adrenal chromaffin cells increases antinociceptive efficacy of xenotransplants without immunosuppression.
AUTHOR: Michalewicz P; Laurito C E; Pappas G D; Lu Y; Yeomans D C
CORPORATE SOURCE: Department of Anatomy and Cell Biology, University of Illinois at Chicago, 60612, USA.
CONTRACT NUMBER: DA08526 (NIDA)
NS28931 (NINDS)
SOURCE: Cell transplantation, (1999 Jan-Feb) Vol. 8, No. 1, pp. 103-9.
Journal code: 9208854. ISSN: 0963-6897.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 27 Jul 1999
Last Updated on STN: 27 Jul 1999
Entered Medline: 15 Jul 1999

AB We have found that immunosuppression is necessary for the survival of xenogeneic adrenal medullary transplants. Because chromaffin cells are essentially nonimmunogenic, it is likely that the highly immunogenic "passenger" cells in the transplant preparation bring about rejection. This article describes a procedure that produces an essentially pure preparation of chromaffin cells for transplantation. Bovine adrenal medullary cells were isolated and differentially plated, resulting in a semipurified preparation of chromaffin cells. Ferromagnetic beads were added to the cell suspension, some of which were phagocytized by endothelial cells, which allowed their removal by exposure to a magnet. The remaining cells were then exposed to ferromagnetic beads coated with **isolectin** B4 from Griffonia simplicifolia and once again to a magnetic field. The "semipurified" preparation contained approximately 90% chromaffin cells, whereas the "highly purified" preparation was > 99.5% chromaffin cells as determined immunohistochemically. The immunogenicity of the two cell preparations was assessed in vitro by determining their capacity to evoke lymphocyte proliferation. Rat spleen lymphocytes were mixed with either a highly purified or semipurified population of bovine

chromaffin cells. The results of this assay demonstrated that the highly purified preparation was a much weaker stimulant of lymphocyte proliferation than was the semipurified preparation and may demonstrate better graft survival in vivo. Transplantation via intrathecal catheter of either 80,000 or 250,000 cells from the highly or partially purified preparations onto the lumbar spinal cord of nonimmunosuppressed and non-nicotine-stimulated rats produced a cell number-dependent antinociception for both A(delta) and **C fiber**-mediated thermonociception at 6 days after transplantation. After 6 days and up to 28 days, only the "highly purified" preparation showed antinociception. These results suggest that nearly complete purification of bovine chromaffin cells minimizes immunorejection of xenogeneic transplants of these cells.

L20 ANSWER 26 OF 32 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1998:277425 SCISEARCH
THE GENUINE ARTICLE: ZF788
TITLE: A distinct subgroup of small DRG cells express GDNF receptor components and GDNF is protective for these neurons after nerve injury
AUTHOR: Bennett D L H; Michael G J; Ramachandran N; Munson J B; Averill S; Yan Q; McMahon S B (Reprint); Priestley J V
CORPORATE SOURCE: St Thomas Hosp, Sch Med, Dept Physiol, Lambeth Palace Rd, London SE1 7EH, England (Reprint); United Med & Dent Sch Guys & St Thomas, Dept Physiol, London SE1 7EH, England; Univ London Queen Mary & Westfield Coll, Dept Anat, London E1 4NS, England; Univ Florida, Coll Med, Dept Neurosci, Gainesville, FL 32610 USA; Amgen Inc, Dept Neurosci, Thousand Oaks, CA 91320 USA
COUNTRY OF AUTHOR: England; USA
SOURCE: JOURNAL OF NEUROSCIENCE, (15 APR 1998) Vol. 18, No. 8, pp. 3059-3072.
ISSN: 0270-6474.
PUBLISHER: SOC NEUROSCIENCE, 11 DUPONT CIRCLE, NW, STE 500, WASHINGTON, DC 20036 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 57
ENTRY DATE: Entered STN: 1998
Last Updated on STN: 1998

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Several lines of evidence suggest that neurotrophin administration may be of some **therapeutic** benefit in the **treatment** of peripheral neuropathy. However, a third of sensory neurons do, not express receptors for the neurotrophins. These neurons are of small diameter and can be identified by the binding of the **lectin** IB4 and the expression of the enzyme thiamine monophosphatase (TMP). Here we show that these neurons express the receptor components for glial-derived neurotrophic factor (GDNF) signaling (RET, GFR alpha-1, and GFR alpha-2). In lumbar dorsal root ganglia, virtually all IB4-labeled cells express RET mRNA, and the majority of these cells (79%) also express GFR alpha-1, GFR alpha-2, or GFR alpha-1 plus GFR alpha-2. GDNF, but not nerve growth factor (NGF), can **prevent** several axotomy-induced changes in these neurons, including the downregulation of IB4 binding, TMP activity, and somatostatin expression. GDNF also **prevents** the slowing of conduction velocity that normally occurs after axotomy in a population of small diameter DRG cells and the A-fiber sprouting

into lamina II of the dorsal horn. GDNF therefore may be useful in the **treatment** of peripheral neuropathies and may protect peripheral neurons that are refractory to neurotrophin **treatment.**

L20 ANSWER 27 OF 32 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 1998132988 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9487020
TITLE: Neurogenic **inflammation** in skin and airways.
AUTHOR: Baluk P
CORPORATE SOURCE: Cardiovascular Research Institute, University of California, San Francisco, USA.
CONTRACT NUMBER: HL-24136 (NHLBI)
SOURCE: The journal of investigative dermatology. Symposium proceedings / the Society for Investigative Dermatology, Inc. [and] European Society for Dermatological Research, (1997 Aug) Vol. 2, No. 1, pp. 76-81. Ref: 56
Journal code: 9609059. ISSN: 1087-0024.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19 Mar 1998
Last Updated on STN: 19 Mar 1998
Entered Medline: 10 Mar 1998

AB Neurogenic **inflammation**, in its original definition, the plasma leakage induced by stimulation of peripheral sensory nerves, occurs in the postcapillary venules of the skin and airways. Plasma leakage is accompanied by increased blood flow, which results from dilatation of arterioles. In skin, these phenomena are manifested as wheal and flare, respectively. Both phenomena are mediated by neuropeptides released from capsaicin-sensitive unmyelinated sensory **nerve fibers.** Substance P is the primary mediator responsible for plasma leakage, acting via tachykinin NK-1 receptors, whereas both calcitonin gene-related peptide and substance P induce vasodilatation. Sensory nerve transmitters also cause release of histamine from mast cells, which contributes substantially to plasma leakage in the skin, but less so in the airways. Substance P causes an increase in vascular permeability as a result of the focal, transient, and fully reversible formation of gaps, approximately 0.5 to 1.5 microns in diameter, located in the intercellular junctions of endothelial cells. The gaps can be visualized by silver nitrate staining of the endothelial cell borders, by **lectin** staining, or by scanning and transmission electron microscopy. Neurogenic **inflammation** can be **inhibited** by **preventing** the stimulation of sensory nerves, by presynaptic **inhibition** of neuropeptide release from sensory nerves, or by blocking neuropeptide receptors. The formation of endothelial gaps can also be **inhibited** by anti-**inflammatory** drugs that stabilize endothelial cells, such as beta-adrenergic agonists and steroids.

L20 ANSWER 28 OF 32 MEDLINE on STN
ACCESSION NUMBER: 97127070 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8971938
TITLE: Enhancement of phagocytosis by calcitonin gene-related peptide (CGRP) in cultured mouse peritoneal

macrophages.
AUTHOR: Ichinose M; Sawada M
CORPORATE SOURCE: Department of Physiology, Shimane Medical University, Izumo, Japan.
SOURCE: Peptides, (1996) Vol. 17, No. 8, pp. 1405-14.
Journal code: 8008690. ISSN: 0196-9781.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 14 Apr 1997
Last Updated on STN: 14 Apr 1997
Entered Medline: 2 Apr 1997

AB Calcitonin gene-related peptide (CGRP) is widely distributed in sensory neurons and **nerve fibers.** To clarify the function of CGRP on the immune system, the effect of CGRP on phagocytosis by peritoneal macrophages was examined by means of flow cytofluorometry. CGRP enhanced phagocytosis of latex beads in a dose-dependent manner. Because the phosphodiesterase **inhibitor** 3-isobutyl, 1-methylxanthine (IBMX) enhanced the CGRP-induced enhancement of phagocytosis, the enhancement might be mediated by cAMP. In the presence of mannan, the phagocytosis was suppressed and the CGRP-induced enhancement was also blocked, suggesting that mannose receptors on macrophages were involved in mediating the phagocytosis of latex beads, and CGRP enhanced the mannose receptor-mediated phagocytosis. The present results indicate that CGRP can **modulate** the function of macrophages in nerve terminals of sensory neurons during the development and maintenance of **inflammation.**

L20 ANSWER 29 OF 32 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 9
ACCESSION NUMBER: 1995:539070 BIOSIS
DOCUMENT NUMBER: PREV199598553370
TITLE: Changes in neuronal markers in a mononeuropathic rat model: Relationship between neuropeptide Y, pre-emptive drug **treatment** and long-term mechanical hyperalgesia.
AUTHOR(S): Munglani, R. [Reprint author]; Bond, A.; Smith, G. D.; Harrison, S. M.; Elliot, P. J.; Birch, P. J.; Hunt, S. P.
CORPORATE SOURCE: Univ. Dep. Anaesthesia, Univ. Cambridge Clin. Sch., Addenbrookes Hosp., Hills Rd., Cambridge CB2 2QQ, UK
SOURCE: Pain, (1995) Vol. 63, No. 1, pp. 21-31.
CODEN: PAINDB. ISSN: 0304-3959.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Dec 1995
Last Updated on STN: 14 Dec 1995

AB Using the chronic constriction model (CCI) of Bennett and Xie (1988), changes in the lumbar spinal cord in neuropeptides and **lectin** IB-4 were examined at 28 days post-nerve constriction and were compared with the degree of mechanical hyperalgesia. Animals following nerve ligation were significantly more hyperalgesic than sham-operated animals (P lt 0.0001). **Lectin** IB-4, a marker of primary afferent **C fibres**, showed a qualitative decrease in staining intensity in laminae 1-2 with ligation compared with both the unoperated contralateral side and with sham animals. Using fluorescent immunohistochemistry to quantify changes in

neuropeptides in the dorsal horn we found that substance P showed significant decreases with ligation compared to sham operation (P lt 0.002). CGRP and galanin showed no significant changes in laminae 1-2 compared to sham-operated animals. Neuropeptide Y (NPY) showed no significant changes in intensity in laminae 1-2; however, in laminae 3-4 there was a significant increase with nerve ligation compared to sham (P lt 0.005). We examined how pre-emptive drug **treatment** affected these neuronal markers at 28 days. We used (1) clonidine, an alpha-2-adrenoreceptor agonist (1 mg/kg, i.p.), (2) morphine, a mu-opioid agonist (5 mg/kg, i.p.) or (3) MK-801, an N-methyl-D-aspartate (NMDA) receptor antagonist (0.3 mg/ kg, s.c.) administered 30 min prior and 6 h following nerve ligation or sham-operation. Hyperalgesia in the ligated group at 28 days was suppressed by **treatment** with pre-emptive clonidine (P = 0.003) or MK-801 (P = 0.003) but not morphine. With the exception of NPY there was no effect of pre-emptive drug **treatment** on any neuronal marker examined. Pre-emptive MK-801 reduced the magnitude of the increase in NPY in laminae 3-4 in the ligated group (P lt 0.005) and clonidine showed a similar trend but this did not reach significance. Morphine had no effect on NPY staining. There was a significant correlation between the increase in NPY staining in laminae 3-4 and the degree of hyperalgesia (r = 0.6, P lt 0.001). These results suggest that the increased NPY expression in laminae 3-4 of the spinal cord (the territory of the myelinated sensory input) may be crucial to the development of hyperalgesia in this model.

L20 ANSWER 30 OF 32 EMBASE

ACCESSION NUMBER: 86215890 EMBASE
DOCUMENT NUMBER: 1986215890
TITLE: Effects of retrograde axonal transport of Ricinus communis agglutinin I on neuroma formation.
AUTHOR: Nennesmo I.; Kristensson K.
CORPORATE SOURCE: Department of Pathology, Division of Neuropathology, Karolinska Institutet, Huddinge Hospital, S-141 86 Huddinge, Sweden
SOURCE: Acta Neuropathologica, (1986) Vol. 70, No. 3-4, pp. 279-283. .
CODEN: ANPTAL
COUNTRY: Germany
DOCUMENT TYPE: Journal
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 1991
Last Updated on STN: 10 Dec 1991

AB The **lectin** Ricinus communis agglutinin I (RCAI) was topically applied to transected mouse sciatic nerve or to neuromas formed 2 months after a nerve transection. Fluorochrome-labelled ricin was transferred to the corresponding dorsal root ganglia where it accumulated selectively in the nerve cells, apparently as a consequence of retrograde axonal transport. The ricin caused an almost total loss of the dorsal root ganglionic neurons and, consequently, could **prevent** formation of neuromas or eliminate an already existing neuroma. The hybrid toxin wheat germ agglutinin (WGA)-ricin-A chain caused no apparent increased sensitivity for neuronal destruction. The drugs doxorubicin and ethidium bromide, similarly applied, labelled satellite and other cells in addition to neurons in the ganglia, and caused only a moderate neuronal loss. The presented method to eliminate neuromas by

selectively destroying sensory neurons may provide a means to study **pain** mechanisms in neuromas.

L20 ANSWER 31 OF 32 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 85300042 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2412270
TITLE: Thin-fiber cutaneous innervation and its intraepidermal contribution studied by labeling methods and neurotoxin **treatment** in rats.
AUTHOR: Kruger L; Sampogna S L; Rodin B E; Clague J; Brecha N; Yeh Y
CONTRACT NUMBER: NS-5685 (NINDS)
SOURCE: Somatosensory research, (1985) Vol. 2, No. 4, pp. 335-56.
Journal code: 8404780. ISSN: 0736-7244.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198510
ENTRY DATE: Entered STN: 20 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 18 Oct 1985

AB Sensory nerves innervating rat distal limb skin were labeled by axonal transport of an enzyme-**lectin** conjugate injected into lumbar dorsal root ganglia (DRG), with emphasis on tracing the course of the thin axons. Selective neonatal neurotoxin destruction of most unmyelinated sensory or sympathetic axons was achieved by **treatment** with capsaicin (CAP) and 6-hydroxydopamine (6-OHDA), respectively. The relationship of substance P-immunoreactive (SPI) axons to the patterns of axonal transport-labeled thin axons was compared in normal and neurotoxin-**treated** animals. SPI is restricted to a limited population of unmyelinated axons, and electron-microscopic observation reveals its total absence in myelinated axons. SPI fibers of sensory origin, as determined by CAP susceptibility, can be traced into the epidermal stratum spinosum, in relation to guard hair follicles, mast cells, and a specific class of small blood vessels. These morphological features are not eliminated by neurotoxin sympathectomy, and some are inferred to contribute to the initial events associated with the neurogenic vasodilation and plasma extravasation associated with the **inflammatory** response. A re-evaluation of the concept of "free nerve endings" is suggested in the context of the variety of afferent and efferent patterns displayed by sensory peptidergic unmyelinated axons, their putative nociceptive role, and the functional diversity of sensory **C fibers.**

L20 ANSWER 32 OF 32 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1985:381409 BIOSIS
DOCUMENT NUMBER: PREV198580051401; BA80:51401
TITLE: SUBUNGUAL GLOMUS TUMOR HISTOPATHOLOGICAL ELECTRON MICROSCOPIC AND IMMUNOCHEMICAL STUDY ON GLOMUS TUMOR CELLS.
AUTHOR(S): CHEN G-S [Reprint author]; YU H-S; SHEN T-C; CHIEN C-H
CORPORATE SOURCE: DEP DERMATOL, KAOSHIUNG MED COLL, KAOSHIUNG, TAIWAN
SOURCE: Taiwan yixuehui zazhi, (1985) Vol. 84, No. 1, pp. 85-95.
CODEN: TIHHAH. ISSN: 0371-7682.
DOCUMENT TYPE: Article

FILE SEGMENT: BA
LANGUAGE: CHINESE

AB Three cases of subungual glomus tumor were studied immunohistochemically and by light microscopy and EM. The immunohistochemical detection of various cell-type characteristics including different types of intermediate filaments and the endothelial cell markers (factor VIII-related antigen (FVIIIR:Ag) and Ulex europaeus I **lectin** (UEAI) binding sites) were carried out. On the immunohistochemical studies, immunofluorescence microscopy and peroxidase antiperoxidase techniques were performed with sections of frozen and formalin-fixed materials (results on frozen sections and formalin-fixed pepsin-**treated** paraffin sections were identical in this study). The glomus cells did not express 2 types of intermediate filament protein, keratin and desmin (the muscle type of intermediate filament protein). Vimentin, the fibroblast type of intermediate filament protein was not available in this study. In the immunohistochemical studies, there were also no 2 types of the endothelial cell markers (FVIIIR:Ag and UEAI) to indicate that the glomus tumor cells were different from normal endothelial cells and endothelial tumor cells. Numerous mast cells were frequently observed among clusters of glomus tumor cells in light microscopy. Meanwhile, EM revealed the non-myelinated **nerve fibers** among the glomus tumor cells and the degranulated mast cells. These mast cells showed moderate metachromasia with Giemsa, toluidine blue, alcian blue and Csaba stains. Mast cells may play a major role in causation of **pain** in the subungual glomus tumor as well as other painful skin tumors such as angioleiomyoma, hemangiopericytoma, hemangioendothelioma, angioblastoma, and pyogenic granuloma, due to the fact that mast cells were also being observed among these tumor cells.

FILE 'MEDLINE' ENTERED AT 13:08:38 ON 02 JUN 2006

FILE LAST UPDATED: 1 JUN 2006 (20060601/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L21	371	SEA	FILE=MEDLINE ABB=ON	PLU=ON	"NERVE FIBERS, UNMYELINATED"/CT
L22	23922	SEA	FILE=MEDLINE ABB=ON	PLU=ON	LECTINS/CT
L23	184	SEA	FILE=MEDLINE ABB=ON	PLU=ON	ERYTHRINA/CT
L24	5	SEA	FILE=MEDLINE ABB=ON	PLU=ON	L21 AND (L23 OR L22)

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L22       23922 SEA FILE=MEDLINE ABB=ON  PLU=ON  LECTINS/CT
L23         184 SEA FILE=MEDLINE ABB=ON  PLU=ON  ERYTHRINA/CT
L25      220998 SEA FILE=MEDLINE ABB=ON  PLU=ON  (PAIN OR ASTHMA OR
               INFLAMMATION OR PSORIASIS OR ULCER)/CT
L26         191 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L22 OR L23) AND L25
L27          20 SEA FILE=MEDLINE ABB=ON  PLU=ON  L26 AND (THERAPY OR
               THERAPEUTIC USE)/CT


=> s l24 or l27
L28          25 L24 OR L27

L28  ANSWER 1 OF 25     MEDLINE on STN
ACCESSION NUMBER:   2005313055     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 15922310
TITLE:              Mu opioid receptor-containing neurons mediate
                    electroacupuncture-produced anti-hyperalgesia in rats
                    with hind paw inflammation.
AUTHOR:             Zhang Rui-Xin; Wang Linbo; Liu Bing; Qiao Jian-Tian;
                    Ren Ke; Berman Brian M; Lao Lixing
CORPORATE SOURCE:   Center for Integrative Medicine, School of Medicine,
                    University of Maryland, 3rd Floor, James Kernan
                    Hospital Mansion, 2200 Kernan Drive, Baltimore, MD
                    21207, USA.
CONTRACT NUMBER:    AT00084 (NCCAM)
SOURCE:             Brain research, (2005 Jun 28) Vol. 1048, No. 1-2, pp.
                    235-40.
                    Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY:       Netherlands
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200509
ENTRY DATE:         Entered STN: 18 Jun 2005
                    Last Updated on STN: 15 Sep 2005
                    Entered Medline: 14 Sep 2005
ED   Entered STN: 18 Jun 2005
     Last Updated on STN: 15 Sep 2005
     Entered Medline: 14 Sep 2005
AB   Previous studies showed that electroacupuncture (EA) significantly
     attenuates inflammatory hyperalgesia in a complete Freund's adjuvant
     (CFA)-induced inflammatory pain rat model. The present study
     demonstrates that pretreatment with Derm-sap, a selective toxin for
     neurons that contain mu opioid receptor (MOR), specifically decreases
     MOR and blocks EA anti-hyperalgesia. These data suggest that spinal
     MOR-containing neurons are involved in the processes by which EA
     produces anti-hyperalgesia.

L28  ANSWER 2 OF 25     MEDLINE on STN
ACCESSION NUMBER:   2005227913     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 15862793
TITLE:              Effects of pertussis toxin on electroacupuncture-
                    produced anti-hyperalgesia in inflamed rats.
AUTHOR:             Liu Bing; Zhang Rui-Xin; Wang Linbo; Ren Ke; Qiao
                    Jian-Tian; Berman Brian M; Lao Lixing
CORPORATE SOURCE:   Center for Integrative Medicine, James Kernan Hospital
                    Mansion, 2200 Kernan Drive, Baltimore, MD 21207, USA.
CONTRACT NUMBER:    AT00084 (NCCAM)
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SOURCE: Brain research, (2005 May 17) Vol. 1044, No. 1, pp. 87-92. Electronic Publication: 2005-04-01. Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200507
ENTRY DATE: Entered STN: 3 May 2005
Last Updated on STN: 16 Jul 2005
Entered Medline: 15 Jul 2005
ED Entered STN: 3 May 2005
Last Updated on STN: 16 Jul 2005
Entered Medline: 15 Jul 2005
AB Our previous study showed that electroacupuncture (EA) significantly attenuated hyperalgesia in an animal model of persistent inflammatory pain. The present study was designed to show if Gi/o protein is involved in EA-produced anti-hyperalgesia. Spinal Gi/o-protein function was destroyed by intrathecal pretreatment with pertussis toxin (PTX). Seven days after the placement of an intrathecal PE-10 tube, PTX was injected into the intrathecal space of the lumbar spinal cord of rats. Seven days after PTX, complete Freund's adjuvant (CFA) was injected into the plantar surface of one hind paw of the rat to induce hyperalgesia in the injected paw. EA treatment was given at acupoint GB30 immediately post-CFA and then hyperalgesia was assessed by measuring the degree of decreased paw withdrawal latency (PWL) to a noxious thermal stimulus. The results showed that PTX pretreatment prevented EA-produced anti-hyperalgesia in the CFA inflammatory pain model but did not affect either baseline pain threshold or CFA-induced hyperalgesia. The data suggest that EA-produced anti-hyperalgesia is mediated by PTX-sensitive Gi/o proteins and the relevant signaling pathways.

L28 ANSWER 3 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2005146305 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15770655
TITLE: C-fiber (Remak) bundles contain both isolectin B4-binding and calcitonin gene-related peptide-positive axons.
AUTHOR: Murinson Beth Brianna; Hoffman Paul Ned; Banihashemi Michael Reza; Meyer Richard Arthur; Griffin John Wesley
CORPORATE SOURCE: Department of Neurology, The Johns Hopkins University School of Medicine, Baltimore, Maryland 21287, USA.. bmurins1@jhmi.edu
CONTRACT NUMBER: NS-41269 (NINDS)
SOURCE: The Journal of comparative neurology, (2005 Apr 18) Vol. 484, No. 4, pp. 392-402. Journal code: 0406041. ISSN: 0021-9967.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200506
ENTRY DATE: Entered STN: 22 Mar 2005
Last Updated on STN: 9 Jun 2005
Entered Medline: 8 Jun 2005
ED Entered STN: 22 Mar 2005
Last Updated on STN: 9 Jun 2005
Entered Medline: 8 Jun 2005
AB Unmyelinated nerve fibers (Remak bundles) in the rodent sciatic nerve

typically contain multiple axons. This study asked whether C-fiber bundles contain axons arising from more than one type of neuron. Most small neurons of the lumbar dorsal root ganglion (DRG) are either glial cell line-derived neurotrophic factor dependent or nerve growth factor dependent, binding either isolectin B4 (IB4) or antibodies to calcitonin gene-related peptide (CGRP), respectively. Injection of IB4-conjugated horseradish peroxidase into a lumbar DRG resulted in intense labeling of IB4 axons, with very low background. Visualized by confocal fluorescence, IB4-binding and CGRP-positive nerve fibers originating from different DRG neurons came together and remained closely parallel over long distances, suggesting that these two types of axon occupy the same Remak bundle. With double-labeling immunogold electron microscopy (EM), we confirmed that IB4 and CGRP axons were distinct and were found together in single Remak bundles. Previous studies indicate that some DRG neurons express both CGRP and IB4 binding. To ensure that our immunogold results were not a consequence of coexpression, we studied large populations of unmyelinated axons by using quantitative single-label EM. Tetramethylbenzidine, a chromogen with strong intrinsic signal amplification of IB4-horseradish peroxidase, labeled as many as 52% of unmyelinated axons in the dorsal root. Concomitantly, 97% of the Remak bundles with more than one axon contained at least one IB4-labeled axon. Probabilistic modeling using binomial distribution functions rejected the hypothesis that IB4 axons segregate into IB4-specific bundles ($P < 0.00001$). We conclude that most Remak bundle Schwann cells simultaneously support diverse axon types with different growth factor dependences.

L28 ANSWER 4 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2004530590 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15500639
TITLE: Anti-vascular endothelial growth factor receptor-2 (Flk-1/KDR) antibody suppresses contact hypersensitivity.
AUTHOR: Watanabe Hideaki; Mamelak Adam J; Wang Binghe; Howell Brandon G; Freed Irwin; Esche Clemens; Nakayama Masashi; Nagasaki Go; Hicklin Daniel J; Kerbel Robert S; Sauder Daniel N
CORPORATE SOURCE: Department of Dermatology, Johns Hopkins University, Baltimore, MD 21287-0900, USA.
SOURCE: Experimental dermatology, (2004 Nov) Vol. 13, No. 11, pp. 671-81.
Journal code: 9301549. ISSN: 0906-6705.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200503
ENTRY DATE: Entered STN: 26 Oct 2004
Last Updated on STN: 25 Mar 2005
Entered Medline: 24 Mar 2005
ED Entered STN: 26 Oct 2004
Last Updated on STN: 25 Mar 2005
Entered Medline: 24 Mar 2005
AB The angiogenic mediator vascular endothelial growth factor (VEGF) and its receptors (VEGFRs) have been studied extensively in neoplastic disease and some inflammatory conditions. Contact hypersensitivity (CHS) is a prototypic Langerhans' cell-dependent, T-helper (Th) 1 cell-mediated inflammatory skin disease that is now also thought to involve angiogenic mediators. The purpose of our study was to examine the role of angiogenesis and VEGF in CHS. We demonstrated that VEGF

production is up-regulated in murine skin after challenge with dinitrofluorobenzene. Administration of a monoclonal antibody directed against the VEGFR-2 (DC101) resulted in a 28.8% decrease in CHS response ($P < 0.001$). Examination of the DC101-treated mouse skin 24 h after challenge revealed decreases in dermal inflammatory cellular infiltrates and total vessel area. Furthermore, mRNA and protein of the Th1-type cytokine interferon (IFN)-gamma was significantly down-regulated in skin of DC101-treated animals 24 h after challenge. The results of the study demonstrate that VEGFR-2 blockade significantly reduces vascular enlargement and edema formation and effects IFN-gamma expression in the skin during challenge in CHS. Our findings suggest that DC101 could function by reducing inflammatory cell migration and hence IFN-gamma expression during the CHS response.

L28 ANSWER 5 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2003608346 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14690482
TITLE: The effects of lectins on indomethacin-induced small intestinal ulceration.
AUTHOR: Yasuoka Takashi; Sasaki Masaya; Fukunaga Tetsuya; Tsujikawa Tomoyuki; Fujiyama Yoshihide; Kushima Ryouji; Goodlad Robert A
CORPORATE SOURCE: Department of Gastroenterology, Shiga University of Medical Science, Otsu, Japan.. yasuoka@belle.shiga-med.ac.jp
SOURCE: International journal of experimental pathology, (2003 Oct) Vol. 84, No. 5, pp. 231-7.
Journal code: 9014042. ISSN: 0959-9673.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 24 Dec 2003
Last Updated on STN: 28 Jan 2004
Entered Medline: 27 Jan 2004
ED Entered STN: 24 Dec 2003
Last Updated on STN: 28 Jan 2004
Entered Medline: 27 Jan 2004
AB Growth factors, such as epidermal growth factor and keratinocyte growth factor, have considerable therapeutic potential for repairing mucosal injury in the intestine when given systemically. Recently, several lectins have been shown to have trophic effects on the intestine when given orally. We examined the effects of phytohaemagglutinin (PHA) and concanavalin A (Con-A) on indomethacin-induced intestinal injury in rat. Five-week-old rats were randomized to four groups (n=5), and intestinal injury was induced by indomethacin injection in three of these groups. Elemental diet (ED) feeding was then commenced. The groups were thus ED feeding/indomethacin untreated (control group), ED feeding/indomethacin treated (ED group), 0.1% PHA-supplemented ED feeding/indomethacin treated (PHA group) and 0.1% Con-A-supplemented ED feeding/indomethacin treated (Con-A group). After 7 days of feeding, macroscopic inflammatory scores, mucosal permeability, myeloperoxidase (MPO) activities and cell proliferation were determined. Macroscopic inflammatory scores, mucosal permeability and MPO activities were significantly lower in both lectin groups than that in control group. Twenty-four hour excretion rate of phenolsulphonphthalein was significantly lower in both lectin groups

than that in ED group. Cell proliferation of the small intestine was significantly increased by both lectins. Lectin supplementation can induce ulcer healing following indomethacin-induced damage.

L28 ANSWER 6 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2003602894 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14685673
TITLE: [Human lectins and their correspondent glycans in cell biology and clinical medicine].
Endogene Lectine des Menschen und ihre Zuckerliganden. Zellbiologische und klinische Bedeutung.
AUTHOR: Kottgen Eckart; Reutter Werner; Tauber Rudolf
CORPORATE SOURCE: Institut fur Laboratoriumsmedizin und Pathobiochemie, Charite-Universitatsmedizin Berlin, Campus Virchow-Klinikum, Berlin.. eckart.koettgen@charite.de
SOURCE: Medizinische Klinik (Munich, Germany : 1983), (2003 Dec 15) Vol. 98, No. 12, pp. 717-38. Ref: 162
Journal code: 8303501. ISSN: 0723-5003.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 20 Dec 2003
Last Updated on STN: 20 Mar 2004
Entered Medline: 19 Mar 2004
ED Entered STN: 20 Dec 2003
Last Updated on STN: 20 Mar 2004
Entered Medline: 19 Mar 2004
AB Lectins are phylogenetically ancient proteins that have specific recognition and binding functions for complex carbohydrates of glycoconjugates, i. e., of glycoproteins, proteoglycans/glycosaminoglycans and glycolipids. This class of proteins mediates important processes of adhesion and communication both inside and outside cells. A large variety of lectins are expressed in the human organism. This article reviews the current knowledge of human lectins with a focus on biochemistry and pathobiochemistry (principles of protein glycosylation and defects of glycosylation as a basis of disease) and cell biology (protein sorting, exocytosis and endocytosis, apoptosis, cell adhesion, cell differentiation, and malignant transformation). The clinical significance of lectin-glycoconjugate interactions is described by example of inflammatory diseases, defects of immune defense, autoimmunity, infectious diseases, and tumor invasion/metastasis. Moreover, therapeutic perspectives of novel drugs that interfere with lectin-carbohydrate interactions are discussed.

L28 ANSWER 7 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2003504435 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14580941
TITLE: Distribution of antinociceptive adenosine A1 receptors in the spinal cord dorsal horn, and relationship to primary afferents and neuronal subpopulations.
AUTHOR: Schulte G; Robertson B; Fredholm B B; DeLander G E; Shortland P; Molander C
CORPORATE SOURCE: Department of Physiology and Pharmacology, Karolinska Institutet, SE-171 77 Stockholm, Sweden.. gunnar.schulte@mbb.ki.se
SOURCE: Neuroscience, (2003) Vol. 121, No. 4, pp. 907-16.

Journal code: 7605074. ISSN: 0306-4522.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 29 Oct 2003
Last Updated on STN: 2 Mar 2004
Entered Medline: 1 Mar 2004
ED Entered STN: 29 Oct 2003
Last Updated on STN: 2 Mar 2004
Entered Medline: 1 Mar 2004
AB Adenosine can reduce pain and allodynia in animals and man, probably via spinal adenosine A1 receptors. In the present study, we investigate the distribution of the adenosine A1 receptor in the rat spinal cord dorsal horn using immunohistochemistry, in situ hybridization, radioligand binding, and confocal microscopy. In the lumbar cord dorsal horn, dense immunoreactivity was seen in the inner part of lamina II. This was unaltered by dorsal root section or thoracic cord hemisection. Confocal microscopy of the dorsal horn revealed close anatomical relationships but no or only minor overlap between A1 receptors and immunoreactivity for markers associated with primary afferent central endings: calcitonin gene-related peptide, or isolectin B4, or with neuronal subpopulations: mu-opioid receptor, neuronal nitric oxide synthase, met-enkephalin, parvalbumin, or protein kinase Cgamma, or with glial cells: glial fibrillary acidic protein. A few adenosine A1 receptor positive structures were double-labeled with alpha-amino-3-hydroxy-5-methyl-4-isoaxolepropionic acid glutamate receptor subunits 1 and 2/3. The results indicate that most of the adenosine A1 receptors in the dorsal horn are located in inner lamina II postsynaptic neuronal cell bodies and processes whose functional and neurochemical identity is so far unknown. Many adenosine A1 receptor positive structures are in close contact with isolectin B4 positive C-fiber primary afferents and/or postsynaptic structures containing components of importance for the modulation of nociceptive information.

L28 ANSWER 8 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2003349447 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12809701
TITLE: Localisation of cannabinoid receptor 1 in rat dorsal root ganglion using in situ hybridisation and immunohistochemistry.
AUTHOR: Bridges D; Rice A S C; Egertova M; Elphick M R; Winter J; Michael G J
CORPORATE SOURCE: Pain Research, Department of Anaesthetics, Faculty of Medicine, Imperial College, Chelsea and Westminster Hospital Campus, London, UK.
SOURCE: Neuroscience, (2003) Vol. 119, No. 3, pp. 803-12.
Journal code: 7605074. ISSN: 0306-4522.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 29 Jul 2003
Last Updated on STN: 13 Sep 2003
Entered Medline: 12 Sep 2003
ED Entered STN: 29 Jul 2003
Last Updated on STN: 13 Sep 2003

Entered Medline: 12 Sep 2003

AB In this study we used in situ hybridisation and double-labelling immunohistochemistry to characterise cannabinoid receptor 1 (CB(1)) expression in rat lumbar dorsal root ganglion (DRG) neurons.Approximately 25% of DRG neurons expressed CB(1) mRNA and displayed immunoreactivity for CB(1). Sixty-nine percent to 82% of CB(1)-expressing cells were also immunoreactive for neurofilament 200, indicative of myelinated A-fibre neurons, which tend to be large- and medium-sized DRG neurons (>600 microm(2)). Approximately 10% of CB1-expressing cells also expressed transient receptor potential vanilloid family ion channel 2 (TRPV2), the noxious heat-transducing channel found in medium to large lightly myelinated Adelta-fibre DRG neurons. Seventeen percent to 26% of CB(1)-expressing cells co-stained using Isolectin B4, 9-10% for calcitonin gene-related peptide and 11-20% for transient receptor potential vanilloid family ion channel 1 (TRPV1), predominantly markers of small non-myelinated C-fibre DRG neurons (<600 microm(2)).These findings suggest that whilst a wide range of DRG neuron phenotypes express CB(1), it is predominantly associated with myelinated fibres.

L28 ANSWER 9 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2003045866 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12522198
TITLE: Differential response properties of IB(4)-positive and -negative unmyelinated sensory neurons to protons and capsaicin.
AUTHOR: Dirajlal Sahera; Pauers Laura E; Stucky Cheryl L
CORPORATE SOURCE: Department of Cell Biology, Neurobiology and Anatomy, Medical College of Wisconsin, Milwaukee 53226-0509, USA.
CONTRACT NUMBER: NS-40538 (NINDS)
SOURCE: Journal of neurophysiology, (2003 Jan) Vol. 89, No. 1, pp. 513-24.
Journal code: 0375404. ISSN: 0022-3077.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 31 Jan 2003
Last Updated on STN: 27 Mar 2003
Entered Medline: 26 Mar 2003

ED Entered STN: 31 Jan 2003
Last Updated on STN: 27 Mar 2003
Entered Medline: 26 Mar 2003

AB Activation of unmyelinated (C-fiber) nociceptors by noxious chemicals plays a critical role in the initiation and maintenance of injury-induced pain. C-fiber nociceptors can be divided into two groups in which one class depends on nerve growth factor during postnatal development and contains neuropeptides, and the second class depends on glial cell line-derived neurotrophic factor during postnatal development and contains few neuropeptides but binds isolectin B(4) (IB(4)). We determined the sensitivity of these two populations to protons and capsaicin using whole cell recordings of dorsal root ganglion neurons from adult mouse. IB(4)-negative unmyelinated neurons were significantly more responsive to protons than IB(4)-positive neurons in a concentration-dependent manner. Approximately 86% of IB(4)-negative neurons responded to pH 5.0 with an inward current compared with only 33% of IB(4)-positive neurons. The subtypes of proton-evoked currents in IB(4)-negative unmyelinated

neurons were also more diverse. Many IB(4)-negative neurons exhibited transient, rapidly inactivating proton currents as well as sustained proton currents. In contrast, IB(4)-positive neurons never displayed transient proton currents and responded to protons only with sustained, slowly inactivating inward currents. The two classes of neurons also responded differently to capsaicin. Twice as many naive IB(4)-negative unmyelinated neurons responded to 1 microM capsaicin as IB(4)-positive neurons, and the capsaicin-evoked currents in IB(4)-negative neurons were approximately fourfold larger than those in IB(4)-positive neurons. Interestingly, proton exposure altered the capsaicin responsiveness of the two classes of neurons in opposite ways. Brief preexposure to protons increased the number of capsaicin-responsive IB(4)-positive neurons by twofold and increased the capsaicin-evoked currents by threefold. Conversely, proton exposure decreased the number of capsaicin-responsive IB(4)-negative neurons by 50%. These data suggest that IB(4)-negative unmyelinated nociceptors are initially the primary responders to both protons and capsaicin, but IB(4)-positive nociceptors have a unique capacity to be sensitized by protons to capsaicin-receptor agonists.

L28 ANSWER 10 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2002418043 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12172656
TITLE: Myelinated and unmyelinated primary afferent axons form contacts with cholinergic interneurons in the spinal dorsal horn.
AUTHOR: Olave M J; Puri N; Kerr R; Maxwell D J
CORPORATE SOURCE: Spinal Cord Group, Institute of Biomedical and Life Sciences, West Medical Building, University of Glasgow, UK.
SOURCE: Experimental brain research. Experimentelle Hirnforschung. Experimentation cerebrale, (2002 Aug) Vol. 145, No. 4, pp. 448-56. Electronic Publication: 2002-06-15.
Journal code: 0043312. ISSN: 0014-4819.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200211
ENTRY DATE: Entered STN: 13 Aug 2002
Last Updated on STN: 5 Jan 2003
Entered Medline: 6 Nov 2002
ED Entered STN: 13 Aug 2002
Last Updated on STN: 5 Jan 2003
Entered Medline: 6 Nov 2002
AB Cholinergic interneurons in laminae III/IV of the dorsal horn contain co-localised gamma-aminobutyric acid (GABA) and frequently form axoaxonic synapses with terminals of primary afferents. They are therefore probably last-order interneurons involved in presynaptic inhibition. The purpose of the present investigation was to determine if these cells receive direct input from primary afferents. Relationships between primary afferents and interneurons were investigated in adult rats. Myelinated primary afferents were labelled with the B-subunit of cholera toxin (CTb). Unmyelinated afferents were labelled with IB4 lectin and an antibody to identify calcitonin-gene-related peptide (CGRP). Cholinergic neurons were labelled with an antibody raised against choline acetyltransferase and examined with a confocal microscope. Cells were reconstructed with NeuroLucida for Confocal and afferent contacts plotted. Interneurons

(N=30) received an average of 20.2+/-11.9 (SD) contacts from CTb-labelled primary afferents, which were preferentially distributed on proximal and intermediate dendrites. Interneurons with dendrites which extended into lamina II (N=20) received an average of 27.4+/-19.0 IB4 contacts (on intermediate and distal dendrites) and 9.2+/-6.8 CGRP contacts. It is concluded that cholinergic interneurons receive contacts from both myelinated and unmyelinated primary afferents and different classes of afferent target particular dendritic domains. Cholinergic interneurons are likely to be components of an inhibitory feedback pathway that is monosynaptically activated by primary afferents.

L28 ANSWER 11 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2002255223 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11994498
TITLE: Unlocking the secrets of galectins: a challenge at the frontier of glyco-immunology.
AUTHOR: Rabinovich Gabriel A; Rubinstein Natalia; Fainboim Leonardo
CORPORATE SOURCE: Division of Immunogenetics, Hospital de Clinicas Jose de San Martin, School of Medicine, University of Buenos Aires, Cordoba 2351, 3er Piso (C 1120), City of Buenos Aires, Argentina.. gabyrabi@ciudad.com.ar
SOURCE: Journal of leukocyte biology, (2002 May) Vol. 71, No. 5, pp. 741-52. Ref: 109
Journal code: 8405628. ISSN: 0741-5400.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 8 May 2002
Last Updated on STN: 31 May 2002
Entered Medline: 30 May 2002
ED Entered STN: 8 May 2002
Last Updated on STN: 31 May 2002
Entered Medline: 30 May 2002
AB Over the last decade, we have witnessed an explosion of information regarding the function of glycoconjugates, carbohydrate-binding proteins, and the elucidation of the sugar code. This progress has yielded not only important insights into fundamental areas of glycobiology but has also influenced other fields such as immunology and molecular medicine. A family of galactoside-binding proteins, called galectins, has emerged recently as a novel kind of bioactive molecules with powerful, immunoregulatory functions. Different members of this family have been shown to modulate positively or negatively multiple steps of the inflammatory response, such as cell-matrix interactions, cell trafficking, cell survival, cell-growth regulation, chemotaxis, and proinflammatory cytokine secretion. To introduce a comprehensive overview of these new advances, here we will explore the molecular mechanisms and biochemical pathways involved in these functions. We will also examine the role of these proteins in the modulation of different pathological processes, such as chronic inflammation, autoimmunity, infection, allergic reactions, and tumor spreading. Understanding the intimate mechanisms involved in galectin functions will help to delineate selective and novel strategies for disease intervention and diagnosis.

L28 ANSWER 12 OF 25 MEDLINE on STN

ACCESSION NUMBER: 1998219461 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9558750
TITLE: The changes of lymphocyte membrane receptors in bronchial asthma and atopic dermatitis in pediatric patients receiving treatment with polyenic fatty acids.
AUTHOR: Gorelova JYu; Semikina E M
CORPORATE SOURCE: Institute of Nutrition, Moscow, Russia.
SOURCE: Zeitschrift fur Ernahrungswissenschaft, (1998) Vol. 37 Suppl 1, pp. 142-3.
Journal code: 0413632. ISSN: 0044-264X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 29 May 1998
Last Updated on STN: 29 May 1998
Entered Medline: 21 May 1998
ED Entered STN: 29 May 1998
Last Updated on STN: 29 May 1998
Entered Medline: 21 May 1998
AB The influence of a diet supplemented with n-3 PUFA on the immune status of children with atopic dermatitis and asthma was investigated. The results of the investigation have shown the improvement of cell immunity along with a decrease in the clinical manifestation of the disease. n-3 PUFA could be used as immunocorrectors in combination with pathogenic treatment of children with allergic diseases.

L28 ANSWER 13 OF 25 MEDLINE on STN
ACCESSION NUMBER: 1998102808 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9439635
TITLE: Epitope mapping of mouse monoclonal antibody EP-5C7 which neutralizes both human E- and P-selectin.
AUTHOR: Tsurushita N; Fu H; Melrose J; Berg E L
CORPORATE SOURCE: Protein Design Labs, Inc., Mountain View, California 94043, USA.. naoya@pdl.com
SOURCE: Biochemical and biophysical research communications, (1998 Jan 6) Vol. 242, No. 1, pp. 197-201.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 24 Feb 1998
Last Updated on STN: 3 Mar 2000
Entered Medline: 12 Feb 1998
ED Entered STN: 24 Feb 1998
Last Updated on STN: 3 Mar 2000
Entered Medline: 12 Feb 1998
AB The epitope of mouse monoclonal antibody (mAb) EP-5C7, which binds to and blocks both human E- and P-selectin, was mapped onto the protein structure of E-selectin. Analyses with E- and L-selectin chimeric proteins and randomly mutagenized E-selectins demonstrated that the EP-5C7 epitope consists of the amino acid residues at positions 21, 22, 23, 119 and 120 of E-selectin. The binding of three neutralizing anti-E-selectin mAb's (E-1E4, H18/7 and CL2), whose epitopes were found to overlap with the E-selectin binding site for carbohydrate

ligands, was not affected by the amino acid substitutions at these five positions. Inspection of the three-dimensional structure of E-selectin indicated that the EP-5C7 epitope is located near the junction between the lectin and EGF-like domains. The ligand binding site was distant from the EP-5C7 epitope, suggesting that the amino acid residues in the EP-5C7 epitope play an important role other than ligand binding in selectin-mediated cell adhesion.

L28 ANSWER 14 OF 25 MEDLINE on STN
ACCESSION NUMBER: 95330258 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7606382
TITLE: Carbohydrate-dependent cell adhesion.
AUTHOR: Fukuda M
CORPORATE SOURCE: Glycobiology Program, La Jolla Cancer Research Foundation, CA 92037, USA.
CONTRACT NUMBER: CA33000 (NCI)
CA33895 (NCI)
CA48737 (NCI)
+
SOURCE: Bioorganic & medicinal chemistry, (1995 Mar) Vol. 3, No. 3, pp. 207-15. Ref: 55
Journal code: 9413298. ISSN: 0968-0896.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 28 Aug 1995
Last Updated on STN: 28 Aug 1995
Entered Medline: 17 Aug 1995
ED Entered STN: 28 Aug 1995
Last Updated on STN: 28 Aug 1995
Entered Medline: 17 Aug 1995

L28 ANSWER 15 OF 25 MEDLINE on STN
ACCESSION NUMBER: 95177821 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7872947
TITLE: [Lectin-based therapy applications from the laboratory to practice].
Lectinbezogene Therapieansatze auf dem Weg vom Labor in die Praxis.
AUTHOR: Gabius H J; Kaltner H
CORPORATE SOURCE: Institut fur Physiologie, Physiologische Chemie und Tierernahrung, Tierarztliche Fakultat, Ludwig-Maximilians-Universitat Munchen.
SOURCE: Berliner und Munchener tierarztliche Wochenschrift, (1994 Nov) Vol. 107, No. 11, pp. 376-81. Ref: 90
Journal code: 0003163. ISSN: 0005-9366.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 7 Apr 1995
Last Updated on STN: 7 Apr 1995
Entered Medline: 28 Mar 1995
ED Entered STN: 7 Apr 1995
Last Updated on STN: 7 Apr 1995

Entered Medline: 28 Mar 1995

AB Thorough analysis of the principles of molecular recognition is the basis for rational development of clinical applications. Currently, our knowledge is expanding, how biological information is encoded in a language of carbohydrate moieties, constituting the glycopart of cellular glycoconjugates. Carbohydrate-binding proteins like lectins can specifically bind these ligands. This glycobiological interplay participates in recognitive inter- and intracellular processes that enable to devise clinical schemes with rational perspective like targeted drug delivery, non-steroidal treatment of inflammation or lectin ligand-dependent treatment of infectious diseases. Besides the ligands, lectins, too, can be of therapeutical value, e.g. as biomodulators in the immune system. The rapid development within glycobiology allows to propose that certain aspects can well find their place in veterinary practice after proving their efficacy in clinical trials.

L28 ANSWER 16 OF 25 MEDLINE on STN
ACCESSION NUMBER: 94325526 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8049406
TITLE: [Role of lectins in allergic reactivity].
Rol' lektinov v allergicheskoi reaktivnosti.
AUTHOR: Chervinskaia T A; Larina O N; Burlakov G V; Ado A D
SOURCE: Biulleten' eksperimental'noi biologii i meditsiny, (1993 Apr) Vol. 115, No. 4, pp. 407-10.
Journal code: 0370627. ISSN: 0365-9615.
PUB. COUNTRY: RUSSIA: Russian Federation
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199409
ENTRY DATE: Entered STN: 14 Sep 1994
Last Updated on STN: 14 Sep 1994
Entered Medline: 2 Sep 1994

ED Entered STN: 14 Sep 1994
Last Updated on STN: 14 Sep 1994
Entered Medline: 2 Sep 1994

AB Skin reaction on phytohemagglutinin in healthy people and in patients with allergic bronchial asthma before and after specific hyposensitization has been studied. The attempt to determine interrelations between the skin sensitivity to phytohemagglutinin and some immunity indexes and to explain several links of lectins' action mechanisms during allergic processes have been made.

L28 ANSWER 17 OF 25 MEDLINE on STN
ACCESSION NUMBER: 78063261 MEDLINE
DOCUMENT NUMBER: PubMed ID: 618692
TITLE: Circulating hyperreactive lymphocytes in bronchial asthma.
AUTHOR: Podleski W K; Grimes J R
SOURCE: Clinical immunology and immunopathology, (1978 Feb) Vol. 9, No. 2, pp. 236-9.
Journal code: 0356637. ISSN: 0090-1229.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197802
ENTRY DATE: Entered STN: 14 Mar 1990
Last Updated on STN: 14 Mar 1990

Entered Medline: 23 Feb 1978
ED Entered STN: 14 Mar 1990
Last Updated on STN: 14 Mar 1990
Entered Medline: 23 Feb 1978

L28 ANSWER 18 OF 25 MEDLINE on STN
ACCESSION NUMBER: 77021192 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1067812
TITLE: Monitoring immune function during immunosuppressive therapy.
AUTHOR: Ziegler J B; Hansen P; Cooper D A; Penny R
SOURCE: Australian and New Zealand journal of medicine, (1976 Apr) Vol. 6, No. 2, pp. 136-41.
Journal code: 1264322. ISSN: 0004-8291.
PUB. COUNTRY: Australia
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197612
ENTRY DATE: Entered STN: 13 Mar 1990
Last Updated on STN: 13 Mar 1990
Entered Medline: 1 Dec 1976
ED Entered STN: 13 Mar 1990
Last Updated on STN: 13 Mar 1990
Entered Medline: 1 Dec 1976
AB Twenty-nine patients with a variety of connective tissue disorders were studied for the effects of immunosuppressive therapy on non-specific parameters of immune function. Baseline studies prior to therapy showed a frequent incidence of anergy (13%) lymphopenia (31%) and abnormal PHA response (43%). Despite these abnormalities in untreated patients it was possible to show an even higher incidence of anergy (31%), lymphopenia (66%) and abnormal PHA response (77%) following immunosuppressive treatment. The changes in lymphocyte count and PHA response were found to be statistically significant. It was found, paradoxically, that delayed hypersensitivity responses improved following institution of therapy in three patients. Clinical efficacy of immunosuppression correlated with lymphopenia and depressed PHA responses; in particular in the five patients with uncontrolled disease, these parameters were normal. Lymphocyte counts and PHA responses are the most simple and informative procedures to monitor immunosuppression in patients.

L28 ANSWER 19 OF 25 MEDLINE on STN
ACCESSION NUMBER: 76136172 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1082767
TITLE: Immunological responses of patients with psoriasis and the effect of treatment with methotrexate.
AUTHOR: Levantine A; Brostoff J
SOURCE: The British journal of dermatology, (1975 Dec) Vol. 93, No. 6, pp. 659-66.
Journal code: 0004041. ISSN: 0007-0963.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197606
ENTRY DATE: Entered STN: 13 Mar 1990
Last Updated on STN: 13 Mar 1990
Entered Medline: 2 Jun 1976
ED Entered STN: 13 Mar 1990

Last Updated on STN: 13 Mar 1990
Entered Medline: 2 Jun 1976

AB A group of thirty-six patients of whom fourteen were being treated with methotrexate, were studied in order to assess T-lymphocyte function by in vitro techniques. Circulating T-lymphocytes in aliqots of blood were assessed by the rosetting technique. No differences were found in psoriatics, whether on methotrexate or not, compared with fifteen control subjects. Lymphocyte counts and lymphocyte transformation to phytohaemagglutinin (PHA) tended to be lower in the psoriatic group as a whole than in the controls, but the differences were not statistically significant, However, a significant inverse relationship was found between the extent of the skin lesions and lymphocyte transformation to PHA, i.e. the smaller the area of skin affected the higher the lymphocyte transformation. Psoriatics treated with methotrexate had fewer skin lesions and higher lymphocyte transformation to PHA than psoriatics not so treated, probably reflecting this inverse relationship. The reason why the presence of extensive psoriasis is associated with depressed lymphocyte transformation is not understood. No evidence was found that methotrexate depressed cell-mediated immunity as judged by these in vitro tests.

L28 ANSWER 20 OF 25 MEDLINE on STN
ACCESSION NUMBER: 76058890 MEDLINE
DOCUMENT NUMBER: PubMed ID: 171932
TITLE: Recent advances in steroid therapy.
AUTHOR: Bach J F
SOURCE: Advances in nephrology from the Necker Hospital, (1975) Vol. 5, pp. 173-200. Ref: 120
Journal code: 0311622. ISSN: 0084-5957.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197601
ENTRY DATE: Entered STN: 13 Mar 1990
Last Updated on STN: 13 Mar 1990
Entered Medline: 29 Jan 1976
ED Entered STN: 13 Mar 1990
Last Updated on STN: 13 Mar 1990
Entered Medline: 29 Jan 1976

L28 ANSWER 21 OF 25 MEDLINE on STN
ACCESSION NUMBER: 74084874 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4589815
TITLE: Lymphocyte characteristics in rheumatic patients and the effect of azathioprine therapy.
AUTHOR: Yy D T; Clements P J; Peter J B; Levy J; Paulus H E; Barnett E V
SOURCE: Arthritis and rheumatism, (1974 Jan-Feb) Vol. 17, No. 1, pp. 37-45.
Journal code: 0370605. ISSN: 0004-3591.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197403

ENTRY DATE: Entered STN: 10 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 22 Mar 1974
ED Entered STN: 10 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 22 Mar 1974

L28 ANSWER 22 OF 25 MEDLINE on STN
ACCESSION NUMBER: 73187054 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4122517
TITLE: Immunopathologic significance of cartilage antigenic components in rheumatoid arthritis.
AUTHOR: Herman J H; Wiltse D W; Dennis M V
SOURCE: Arthritis and rheumatism, (1973 May-Jun) Vol. 16, No. 3, pp. 287-97.
Journal code: 0370605. ISSN: 0004-3591.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197308
ENTRY DATE: Entered STN: 10 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 2 Aug 1973
ED Entered STN: 10 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 2 Aug 1973

L28 ANSWER 23 OF 25 MEDLINE on STN
ACCESSION NUMBER: 72074552 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4331971
TITLE: The effect of plasma cortisol levels on the lymphocyte transformation test.
AUTHOR: Zeman G O; Cohen G; Budrys M; Williams G C; Javor H
SOURCE: The Journal of allergy and clinical immunology, (1972 Jan) Vol. 49, No. 1, pp. 10-5.
Journal code: 1275002. ISSN: 0091-6749.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197203
ENTRY DATE: Entered STN: 10 Mar 1990
Last Updated on STN: 10 Mar 1990
Entered Medline: 6 Mar 1972
ED Entered STN: 10 Mar 1990
Last Updated on STN: 10 Mar 1990
Entered Medline: 6 Mar 1972

L28 ANSWER 24 OF 25 MEDLINE on STN
ACCESSION NUMBER: 72042824 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4399176
TITLE: Lymphocyte transformation with bacterial antigens in intrinsic asthma.
AUTHOR: Virtue C M; Wittig H J; Cook T J
SOURCE: The Journal of allergy and clinical immunology, (1971 Dec) Vol. 48, No. 6, pp. 321-30.
Journal code: 1275002. ISSN: 0091-6749.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197201
ENTRY DATE: Entered STN: 10 Mar 1990
Last Updated on STN: 19 Apr 1995
Entered Medline: 25 Jan 1972
ED Entered STN: 10 Mar 1990
Last Updated on STN: 19 Apr 1995
Entered Medline: 25 Jan 1972

L28 ANSWER 25 OF 25 MEDLINE on STN
ACCESSION NUMBER: 70064165 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4188224
TITLE: Anergy, dysimmunoglobulinemia, and unexplained inflammation. A new therapeutic approach with a chemically defined diet.
AUTHOR: Buckley C E 3rd
SOURCE: The Journal of allergy, (1969 Dec) Vol. 44, No. 6, pp. 355-68.
Journal code: 1305603. ISSN: 0021-8707.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197002
ENTRY DATE: Entered STN: 1 Jan 1990
Last Updated on STN: 6 Feb 1998
Entered Medline: 4 Feb 1970
ED Entered STN: 1 Jan 1990
Last Updated on STN: 6 Feb 1998
Entered Medline: 4 Feb 1970

FILE 'HOME' ENTERED AT 13:14:09 ON 02 JUN 2006

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=> d his ful

     (FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
     JICST-EPLUS, JAPIO' ENTERED AT 12:45:21 ON 02 JUN 2006)
                DEL HIS Y

     FILE 'REGISTRY' ENTERED AT 12:47:19 ON 02 JUN 2006

     FILE 'REGISTRY' ENTERED AT 12:47:40 ON 02 JUN 2006
                E ERYTHRINA LECTIN/CN 5
L1              1 SEA ABB=ON  PLU=ON  "ERYTHRINA CRISTA-GALLI, EXT."/CN

     FILE 'HCAPLUS' ENTERED AT 12:47:52 ON 02 JUN 2006
L*** DEL     2658 S L1 OR ERYTHRINA(S)(LECTIN OR CRISTAGALLI OR CRISTA GALLI)
L*** DEL       13 S L2 AND (C OR NERVE)(3A)(FIBER OR FIBRE)
                  D KWIC
L2            298 SEA ABB=ON  PLU=ON  L1 OR ERYTHRINA(S)(LECTIN OR CRISTAGALL
                  I OR CRISTA GALLI) OR ECL(S)ERYTHRINA
L3              2 SEA ABB=ON  PLU=ON  L2 AND (C OR NERVE)(3A)(FIBER OR
                  FIBRE)
                  D QUE L3
                  D L3 1-2 .BEVSTR

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
     JICST-EPLUS, JAPIO' ENTERED AT 12:49:24 ON 02 JUN 2006
L4              4 SEA ABB=ON  PLU=ON  L3
L5              4 DUP REM L4 (0 DUPLICATES REMOVED)
                  D 1-4 IBIB ABS

     FILE 'HCAPLUS' ENTERED AT 12:50:38 ON 02 JUN 2006
L6             11 SEA ABB=ON  PLU=ON  L2 AND (PAIN OR ACHE OR INFLAMMAT? OR
                  PSORIASIS OR ASTHMA OR ULCER OR HEADACHE OR MUCUS(3A)(HYPER
                  SECRET? OR HYPER SECRET?) OR PUSTUL? OR HEMICRANIA## OR
                  HEMI CRANIA## OR CEPHALGIA)
L7              6 SEA ABB=ON  PLU=ON  L6 AND (TREAT? OR THERAP? OR PREVENT?)

                  D QUE L7
L8              5 SEA ABB=ON  PLU=ON  L7 NOT L3
                  D 1-5 .BEVSTR

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
     JICST-EPLUS, JAPIO' ENTERED AT 12:51:57 ON 02 JUN 2006
L9             15 SEA ABB=ON  PLU=ON  L7
L10            13 SEA ABB=ON  PLU=ON  L9 NOT L4
L11             8 DUP REM L10 (5 DUPLICATES REMOVED)
                  D 1-8 IBIB ABS

     FILE 'REGISTRY' ENTERED AT 12:54:07 ON 02 JUN 2006
                E LECTIN/CN 5
                E LECTINS/CN 5
L12           664 SEA ABB=ON  PLU=ON  (LECTINS OR LECTIN ?)/CN

     FILE 'HCAPLUS' ENTERED AT 12:54:34 ON 02 JUN 2006
L13         40420 SEA ABB=ON  PLU=ON  L12 OR LECTIN OR ISOLECTIN
L14            90 SEA ABB=ON  PLU=ON  L13 AND (C OR NERVE)(3A)(FIBER OR
                  FIBRE)
L15            34 SEA ABB=ON  PLU=ON  L14 AND (PAIN OR ACHE OR INFLAMMAT? OR
                  PSORIASIS OR ASTHMA OR ULCER OR HEADACHE OR MUCUS(3A)(HYPER
                  SECRET? OR HYPER SECRET?) OR PUSTUL? OR HEMICRANIA## OR
                  HEMI CRANIA## OR CEPHALGIA)
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L16          14 SEA ABB=ON  PLU=ON  L15 AND (TREAT? OR THERAP? OR MODULAT?
                OR PREVENT? OR INHIBIT?)
                D QUE L16
L17          13 SEA ABB=ON  PLU=ON  L16 NOT (L3 OR L7)
                D 1-13 .BEVSTR

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
     JICST-EPLUS, JAPIO' ENTERED AT 13:03:45 ON 02 JUN 2006
L18          54 SEA ABB=ON  PLU=ON  L16
L19          52 SEA ABB=ON  PLU=ON  L18 NOT (L4 OR L9)
L20          32 DUP REM L19 (20 DUPLICATES REMOVED)
                D 1-32 IBIB ABS

     FILE 'MEDLINE' ENTERED AT 13:08:38 ON 02 JUN 2006
                E "NERVE FIBERS, UNMYELINATED"/CT 5
L21         371 SEA ABB=ON  PLU=ON  "NERVE FIBERS, UNMYELINATED"/CT
                E LECTINS/CT 5
L22       23922 SEA ABB=ON  PLU=ON  LECTINS/CT
                E ERYTHRINA/CT
L23         184 SEA ABB=ON  PLU=ON  ERYTHRINA/CT
L24           5 SEA ABB=ON  PLU=ON  L21 AND (L23 OR L22)
L25      220998 SEA ABB=ON  PLU=ON  (PAIN OR ASTHMA OR INFLAMMATION OR
                PSORIASIS OR ULCER)/CT
L26         191 SEA ABB=ON  PLU=ON  (L22 OR L23) AND L25
L*** DEL     41 S L26 AND (THERAPY OR THERAPEUTIC)
L*** DEL      0 S (L22 OR L23)(L)L25
L27          20 SEA ABB=ON  PLU=ON  L26 AND (THERAPY OR THERAPEUTIC
                USE)/CT
                D QUE L24
                D QUE L27
L*** DEL    194 S L24 OR L26
L*** DEL      0 S L24 AND L27
L28          25 SEA ABB=ON  PLU=ON  L24 OR L27
                D 1-25 .BEVERLYMED

     FILE 'HOME' ENTERED AT 13:14:09 ON 02 JUN 2006


     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:    1 JUN 2006  HIGHEST RN 886490-27-3
     DICTIONARY FILE UPDATES:   1 JUN 2006  HIGHEST RN 886490-27-3

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

       Please note that search-term pricing does apply when
       conducting SmartSELECT searches.

     ************************************************************
     *                                                          *
     * The CA roles and document type information have been removed from *
     * the IDE default display format and the ED field has been added,   *
     * effective March 20, 2005.  A new display format, IDERL, is now    *
     * available and contains the CA role and document type information. *
     *                                                          *
     ************************************************************
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Searcher : Shears 571-272-2528

Structure search iteration limits have been increased. See HELP SLIMI for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE HCAPLUS

FILE COVERS 1907 - 2 Jun 2006 VOL 144 ISS 24
FILE LAST UPDATED: 1 Jun 2006 (20060601/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE MEDLINE
FILE LAST UPDATED: 1 JUN 2006 (20060601/UP). FILE COVERS 1950 TO DAT

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.ht
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 31 May 2006 (20060531/ED)

Searcher : Shears 571-272-2528

FILE EMBASE
FILE COVERS 1974 TO 2 Jun 2006 (20060602/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE WPIDS
FILE LAST UPDATED: 26 MAY 2006 <20060526/UP>
MOST RECENT DERWENT UPDATE: 200634 <200634/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html a
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<

FILE CONFSCI
FILE COVERS 1973 TO 10 Apr 2006 (20060410/ED)

CSA has resumed updates, see NEWS FILE

FILE SCISEARCH

FILE COVERS 1974 TO 1 Jun 2006 (20060601/ED)

SCISEARCH has been reloaded, see HELP RLOAD for details.

FILE JICST-EPLUS
FILE COVERS 1985 TO 30 MAY 2006 (20060530/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

FILE JAPIO
FILE LAST UPDATED: 3 APR 2006 <20060403/UP>
FILE COVERS APRIL 1973 TO DECEMBER 22, 2005

>>> GRAPHIC IMAGES AVAILABLE <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOT YET AVAILABLE IN THIS FILE. USE IPC7 FORMAT FOR SEARCHING THE IPC. WATCH THIS SPACE FOR FURTHE DEVELOPMENTS AND SEE OUR NEWS SECTION FOR FURTHER INFORMATION ABOUT THE IPC REFORM <<<

FILE HOME